RESEARCH ARTICLE

An Observational Study to Estimate the Prevalence of Subclinical Hypothyroidism and Anti-TPO Antibodies in Pregnancy and to Compare the Maternal and Fetal Outcomes with Euthyroid Cases

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Abstract

Introduction: Thyroid disorders, the second most common endocrinologic issue in pregnant women, even get extended to subclinical hypothyroidism (SCH), which is a condition associated with the risk of pregnancy complications and also adverse effects on the baby's neuropsychological development. This study aims to assess the frequency of SCH and anti-TPO antibodies in pregnant women and compare the outcomes to those of women without thyroid issues.

Materials and methods: A hospital-based observational study was conducted as an observational study in a tertiary teaching hospital, 500 pregnant women aged 18–40 underwent thyroid functioning and anti-TPO antibody testing. Cases were managed on the basis of their thyroid and TPO statuses, with comprehensive follow-ups tracking maternal details during antenatal, intrapartum, and postpartum periods, too. Neonatal outcomes, including APGAR scores, Neonatal Intensive Care Unit (NICU) care, and baby weights was documented. Neonatal S.TSH levels were assessed post-birth.

Results: Prevalence rates in our study were 32% for SCH, 1.98% for overt hypothyroidism, and 66.02% for euthyroid cases. Out of the 184 patients with SCH, 85 (46.20%) tested positive for anti-TPO antibodies. Women with SCH exhibited a significantly higher rate of cesarean sections; SCH with anti-TPO-Ab positivity correlated notably with preterm delivery, premature rupture of membranes, and hyperbilirubinemia.

Conclusion: The study shows that one in three antenatal care patients screened for thyroid disorders was diagnosed with SCH. The condition is linked to complications including an increased incidence of elevated cesarean section rates and NICU admissions compared to pregnant women with a euthyroid state.

Clinical significance: Testing for thyroid function and anti-TPO ought to be a routine for every pregnant woman so that they can promptly identify SCH and prevent potential complications associated with pregnancy.

Keywords: Anti-TPO antibodies, Fetal outcome, Levothyroxine, Maternal outcome, Subclinical hypothyroidism.

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Introduction

Among endocrinological disorders, thyroid disorders rank second among pregnant women. In pregnancy, overt hypothyroidism is estimated to occur at 0.3–0.5%. The statistics state that 2–3% of pregnant women suffer from subclinical hypothyroidism (SCH), while 0.1–0.4% of pregnant women suffer from hyperthyroidism.[1]

Women with thyroid disorders have a higher probability of developing – threatened abortion, preeclampsia, preterm labor, placental abruption, and postpartum hemorrhage. Babies born to mothers with untreated thyroid disorders are more prone to low birth weight, preterm delivery, fetal or neonatal hyperthyroidism, fetal growth retardation, high stillbirth, neonatal deaths, neonatal hyperbilirubinemia, neonatal hypothyroidism, and perinatal mortality.[2]

Immediate treatment is required for women with overt thyroid disorders to prevent maternal and fetal complications. Such women must be prescribed levothyroxine for a better maternal and fetal outcome.[3–6]

Subclinical hypothyroidism is defined by an increased concentration of S.TSH with normal levels of thyroxine (T4) and triiodothyronine (T3). Studies have suggested that women suffering from SCH and not on levothyroxine are more prone to an adverse maternal and perinatal outcome.[7]

Researchers have found that 73% of patients suffering from SCH also had raised thyroid peroxidase (TPO) antibodies. A rapid

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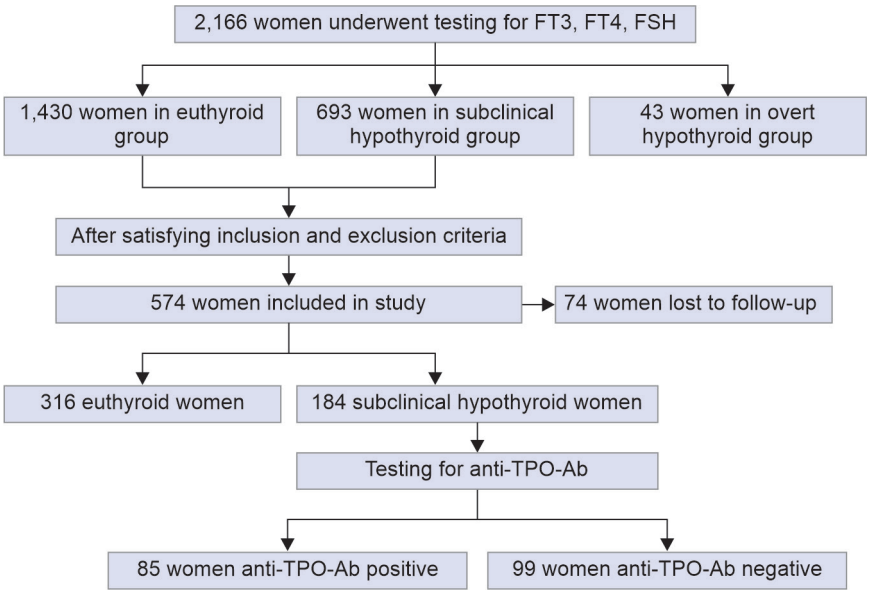


Fig. 1: The flowchart demonstrates the outline for our study

decline in thyroid function is associated with a higher value of TPO antibody. Data suggests that women with SCH not on medication get converted to overt hypothyroidism at a 5% conversion rate per year.[7] Hence, it is of utmost importance that screening and diagnosis are provided to the patients. Studies demonstrate that patients with SCH with anti-TPO antibody positivity should be treated with levothyroxine.[3–6]

Hence the study was done at our tertiary care center to ascertain the prevalence of SCH and TPO antibodies in pregnancy and to compare the maternal and fetal outcomes in SCH vs euthyroid cases.

Materials and Methods

At our tertiary care teaching hospital, we conducted an observational study including 500 singleton pregnant women, aged between 18 and 40 years. Hyperthyroid cases, cases with co-morbidities (diabetes, hypertension), and women with S.TSH values >4 mIU/mL did not form part of our study. Women presently on any thyroid medication, history of thyroid replacement therapy, and treatment with drugs interfering with thyroid function were also excluded.

The patients were divided as per the free T3, T4, and TSH values into the following groups as per American Thyroid Association (ATA) 2017 guidelines:[6] Euthyroid women – values normal FT3, FT4, S.TSH values. Subclinical hypothyroid – values as S.TSH 2.5 to 4.0 μIU/mL, FT4 values between 0.7 and 1.9 ng/dL (normal range); overt hypothyroid – values > 4 μIU/mL. Participants of the study with SCH underwent anti-TPO testing.

As per the ATA guidelines,[6] those patients with S.TSH within the range of 2.5–4 μIU/mL and positive for anti-TPO – were started on treatment with T. levothyroxine. Those patients with anti-TPO negative and S.TSH values from 2.5 to 4 μIU/mL were not given any treatment. However, during their antenatal course, levothyroxine was started when S.TSH levels exceeded >4 μIU/mL on trimester-wise monitoring.

The enrolled patients were followed through their ANC period, and their S.TSH levels were tested once every 3 months and maintained in the trimester-specific ranges by changing the dose of levothyroxine. Their antenatal period was monitored for any medical and obstetric complications. Their detailed intrapartum and postpartum history was maintained. The neonatal outcome in terms of APGAR at birth, need for Neonatal Intensive Care Unit (NICU) care, and baby weight was noted. At birth, Neonatal S.TSH was sent and noted.

Statistical analysis was done using SPSS ver. 26 using appropriate tests. Graphical representation was done using MS Excel 2021.

Results

A total of 2,166 pregnant women attending the ANC OPD were screened for thyroid disorders by free triiodothyronine (T3), free thyroxine (T4), and TSH. As per the values obtained, the number of subclinical hypothyroid, overt hypothyroid, and euthyroid patients was 693, 43, and 1,430, respectively. Our study demonstrates SCH to be present among 32% of pregnant women; overt hypothyroidism and euthyroidism in our study were 1.98 and 66.02%, respectively. A total of 574 women satisfied the eligibility criteria; of them, 74 were lost to follow-up, so final data analysis was done on 500 cases. Among these 500 cases, 316 (63.2%) were euthyroid and 184 (36.8%) were SCH cases (Figs 1 and 2). A total of 85 out of 184 SCH cases (46.2%) showed anti-TPO antibody positivity and started on levothyroxine (Fig. 3).

The mean age of subclinical hypothyroid patients was 24.99 ± 2.42 years and that of euthyroid patients was 24.39 ± 2.23 years ($p < 0.05$). The incidence of Cesarean section as a mode of delivery demonstrated a statistically significant increase in women with SCH (34.24 vs 31.65%; $p < 0.05$). Subclinical hypothyroidism with anti-TPO Ab positivity was notably linked to preterm delivery (9.22%) along with premature rupture of membranes (11.76%) ($p < 0.05$) (Fig. 4). No disparity was found in preterm delivery between SCH with anti-TPO Ab negativity (8.02%) and euthyroid women (7.92%). The incidence of premature rupture of membranes in women with SCH with anti-TPO Ab negatives (5.54%) and euthyroid women (3.16%) was not statistically significant. No significant difference among gestational hypertension, gestational diabetes mellitus, and fetal growth restriction was noted among the three groups ($p > 0.05$).

Among babies born to mothers with SCH with Anti TPO Ab positive, the average birth weight was 2.31 ± 0.40 kg, SCH with

anti-TPO Ab negative was 2.63 ± 0.38 kg and in euthyroid cases was 2.74 ± 0.21 kg ($p < 0.05$). The mean APGAR score of neonates of all three groups did not demonstrate a significant difference ($p > 0.05$). As demonstrated by Figure 5, hyperbilirubinemia was found to be statistically significant in neonates born to mothers with SCH with both anti-TPO Ab positive (17.65%) and anti-TPO Ab negative (16.16%) when compared to women belonging to the euthyroid group (6.33%) ($p < 0.05$). The requirement of NICU stay (11.76%) was also higher in women with SCH and anti-thyroid peroxidase antibody positivity ($p < 0.05$).

The mean serum TSH of neonates born to mothers with SCH with anti-TPO Ab positive was 9.36 ± 6.49 µIU/mL, in SCH with anti-TPO Ab negative was 9.26 ± 7.17 µIU/mL and in the euthyroid group was 6.12 ± 6.31 µIU/mL ($p > 0.05$) as demonstrated by Figure 6.

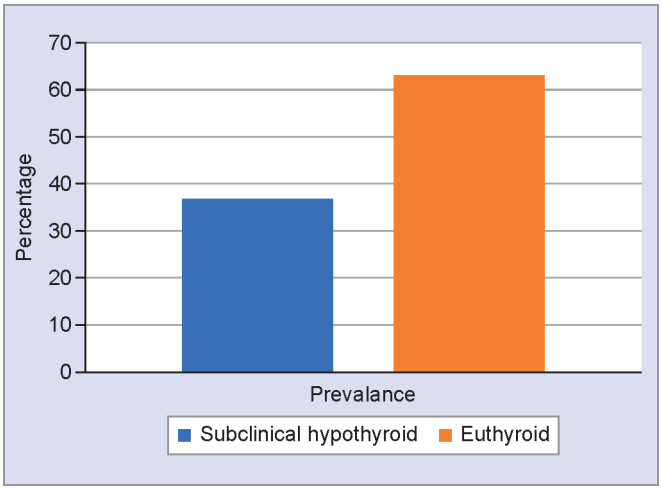


Fig. 2: Prevalence of subclinical hypothyroid, euthyroid in our study

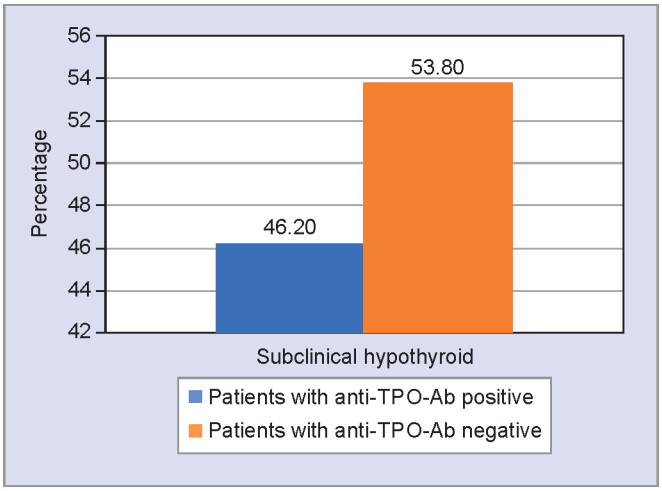
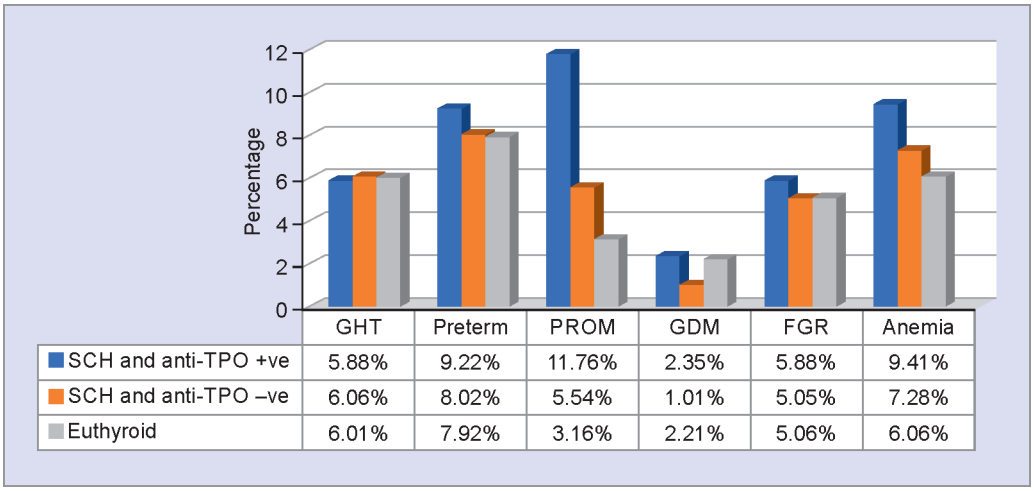


Fig. 3: Comparison according to the presence of anti-TPO antibody in subclinical hypothyroid group

Discussion

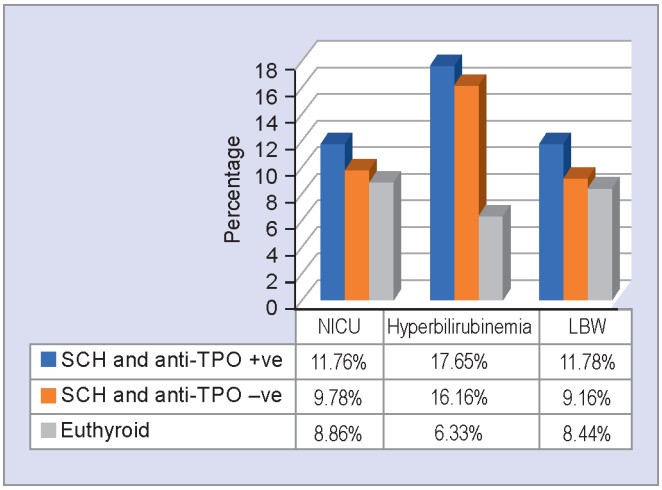
In our study, we observed the prevalence of euthyroid state as 66.02%, SCH as 32%, and overt hypothyroidism as 1.98%. Rehman and Gul.[8] hospital-based prospective comparative study found the prevalence of SCH was 14.3% and the prevalence of euthyroid women was 85.7%. Goel et al.[9] revealed that the occurrence of SCH stands at 32.5%. In the study, it was also observed that overt hypothyroidism had a prevalence of 1.3%, while euthyroid women constituted 66.2% of the population. Li et al.[10] study found based on the 2017 ATA criteria, out of 1,556 women there were 1,404 euthyroid women (90.23%) and 152 SCH pregnant women (9.77%). Bhattacharyya et al.[11] prospective study found the incidence of SCH was 5.25% (21 out of 400) and euthyroid women were 94.75%. Mahadik et al.[12] conducted a comprehensive observational study, revealing a prevalence of 5.6% for subclinical hypothyroidism, 3.5% for overt hypothyroidism, 1.5% for subclinical hyperthyroidism, and 89.4% for euthyroid women. These studies indicate a higher prevalence of SCH than previously thought.

In our current investigation, it was observed that 46.2% of women with SCH tested positive for anti-TPO Ab, while 53.8% of patients with SCH were found to be negative for anti-TPO Ab. In their prospective study on 400 antenatal mothers, Bhattacharyya et al. found an 11.5% incidence rate of anti-TPO-Ab positivity in the first trimester. Among euthyroid mothers, 11.34% (43 out of 379) tested positive, and in cases of subclinical hypothyroid antenatal mothers, the positivity rate was 14.28% (3 out of 21). In a prospective observational study by Goel et al.,[9] anti-TPO Ab was found in 28.35% of women with subclinical hypothyroidism. In a



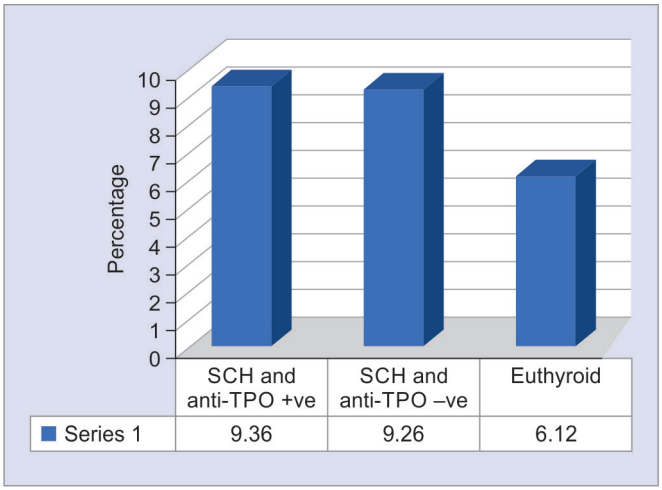
	GHT	Preterm	PROM	GDM	FGR	Anemia
SCH and anti-TPO +ve	5.88%	9.22%	11.76%	2.35%	5.88%	9.41%
SCH and anti-TPO –ve	6.06%	8.02%	5.54%	1.01%	5.05%	7.28%
Euthyroid	6.01%	7.92%	3.16%	2.21%	5.06%	6.06%

Fig. 4: Comparison of patients according to maternal complications



	NICU	Hyperbilirubinemia	LBW
SCH and anti-TPO +ve	11.76%	17.65%	11.78%
SCH and anti-TPO –ve	9.78%	16.16%	9.16%
Euthyroid	8.86%	6.33%	8.44%

Fig. 5: Comparison of patients according to fetal outcome



	SCH and anti-TPO +ve	SCH and anti-TPO –ve	Euthyroid
Series 1	9.36	9.26	6.12

Fig. 6: Comparison of mean serum TSH levels of neonates

prospective observational study by Kiran et al.,[13] anti-TPO Ab was present in 22.3% of women with subclinical hypothyroidism, while 77.7% tested negative for anti-TPO Ab. In the study by Rajput et al.,[14] 39.4% of women with SCH tested positive for anti-TPO antibody, while 60.6% tested negative.

Our study noted a significantly higher cesarean section rate in women with SCH (34.24 vs 31.65%). Sreelatha et al.[15] prospective study found LSCS in 22.9% of cases and FTND was 77.1%. A comparative study by Rehman and Gul[8] found that normal deliveries occurred in 36.00% and cesarean deliveries in 64%. In comparison, euthyroid pregnant women experienced normal deliveries in 74.67% and caesarean deliveries in 25.33%. Mahadik et al.[12] observational study showed a significant association was noted as cesarean delivery transpired in 26.3% of women with hypothyroidism.

Our study indicates a significant association between preterm delivery (9.22%) and SCH with anti TPO–Ab positivity when compared to both anti-TPO-Ab-negative women with SCH (8.02%) and the euthyroid group (7.92%). Subclinical hypothyroidism with anti-TPO-Ab positivity exhibited a notable association with premature rupture of membranes (11.76%) compared to both Anti-TPO Ab-negative women with SCH (5.54%) and women in the euthyroid group (3.16%). In the study led by Bhattacharyya et al.,[11] 16.66% of participants with anti-TPO Ab positivity developed gestational hypertension, while 9.19% with anti-TPO Ab negativity experienced gestational hypertension. Moreover, 14.28% of mothers positive for anti-TPO-Ab had preterm delivery. In the observational study by Mahadik et al.,[12] complications observed in mothers with subclinical hypothyroidism and anti-TPO-Ab positivity included gestational hypertension (15.8%), preterm delivery (5.3%), and anemia (26.3%). In the prospective study conducted by Sreelatha et al.,[15] maternal complications were observed among 96 cases of subclinical hypothyroidism. These included oligohydramnios in 16.7% of cases, hypertensive disorders in pregnancy in 14.7% of cases, gestational diabetes mellitus in 4.2% of cases, pre-term labor in 3.1% of cases, and postpartum hemorrhage (PPH) in 6.3% of cases. Shruthi et al.[16] demonstrated in their study reported complications noted in mothers with SCH as follows: in mothers with SCH and anti-TPO Ab positive, gestational hypertension was seen in 5.2% of patients, preterm delivery in 1%, GDM in 22.3%, and fetal growth restrictions in 7.4% of patients. In mothers with SCH and anti-TPO Ab negative, gestational hypertension was seen in 9.6% of patients, preterm delivery in 1%, GDM in 10.5%, and fetal growth restrictions in 1.3% of patients.

In our investigation, hyperbilirubinemia exhibited statistical significance in women with SCH, both with anti-TPO–Ab positivity (17.65%) and anti-TPO Ab–negativity (16.16%), compared to women in the euthyroid group (6.33%), as determined by the analysis of variance (ANOVA) test ($p < 0.05$). In our study, the necessity for NICU stay (11.76%) and the prevalence of low birth weight (11.78%) were notably elevated in the SCH group with Anti-TPO Ab positivity ($p < 0.05$). This is similar to the studies of Bathula and Kathari[17] Sreelatha et al.,[15] and Rehman et al.[8] In the prospective study led by Sreelatha et al.,[15] the observations revealed that 21.9% of cases had infants with low birth weight (LBW). Additionally, 9.4% of cases had infants with hyperbilirubinemia, 3.1% experienced premature birth, and 14.6% had infants requiring admission to the NICU. Mahadik K et al.[12] conducted an observational study and reported complications noted in neonates born to mothers with SCH as follows: 5.3% of neonates had premature birth, 42.1% had NICU admission, and 31.6% had low birth weight. Shruthi et al.,[16] in their study, demonstrated NICU admission in 1% of patients. Premature births were seen in 5.2% of neonates born to mothers who had SCH with anti-TPO Ab positive and in 9.6% of neonates born to mothers who had SCH with anti-TPO Ab negative.

The mean birth weight in SCH with Anti TPO Ab positive was 2.31 ± 0.40 kg, SCH with anti-TPO Ab negative was 2.63 ± 0.38 kg, and in euthyroid cases was 2.74 ± 0.21 kg ($p < 0.05$). Rehman et al.[8] hospital-based prospective comparative study found incidence of LBW as 36% in SCH patient, as compared to 26.6% in euthyroid patients. Mahadik et al.[12] observational study observed that 31.6% of SCH cases had LBW babies, and the association was significant.

The mean serum TSH of neonates born to mothers in the SCH with anti-TPO Ab positive was 9.36 ± 6.49 µIU/mL, in SCH with anti-TPO Ab negative was 9.26 ± 7.17 µIU/mL and in the euthyroid group was 6.12 ± 6.31 µIU/mL ($p > 0.05$). Parallel investigations by Shravani et al.,[18] Kiran et al.,[19] and Pai et al.[20] yielded comparable outcomes, indicating no significant difference in S.TSH levels among neonates born to hypothyroid mothers.

Conclusion

One out of three ANC patients screened for thyroid disorders was found to have subclinical hypothyroidism. A substantial number

of women with subclinical hypothyroid state tested positive for anti-TPO Ab. A troubling association emerged in these cases: a marked rise in premature births, babies with alarmingly LBWs, and a concerning increase in NICU admissions. Notably, these outcomes contrasted starkly with those observed in pregnant women who tested negative for TPO antibodies and maintained a euthyroid state. Hence all women with SCH must undergo anti-TPO antibody testing to determine the need for starting levothyroxine therapy.

Clinical Significance

Subclinical hypothyroidism, often cloaked in normalcy, can cast a long shadow over pregnancy, potentially leading to premature births, newborns struggling with low birth weight, and the unsettling symphony of NICU monitors. Yet, a simple blood test – a glance at thyroid function and TPO antibodies – can disarm this threat. Early detection and treatment with levothyroxine offer a shield against these complications, ensuring a smoother sailing for both mother and child. From a resource-conscious perspective, proactive screening for SCH during pregnancy emerges as a sound investment. The relatively low cost of thyroid function and TPO antibody testing pales in comparison to the potential financial burden associated with managing premature births, low birth weight infants, and prolonged NICU stays. By nipping adverse outcomes in the bud through early intervention, we not only improve maternal and fetal health but also optimize healthcare resource allocation.

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