

Subclinical Hypothyroidism in Pregnancy: An Overview of Literature and Guidelines

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Abstract

Review Article

The prevalence of overt and subclinical hypothyroidism (SCH) during pregnancy is reported to be 0.3-0.5% and 2-3% respectively. In about 5-18% of reproductive women, thyroid autoantibodies are present. Thyroid dysfunction (hypothyroidism, hyperthyroidism and autoimmune diseases) during pregnancy can lead to serious problems for both mother and baby. The multitude of adverse events associated with untreated thyroid disease during pregnancy leads to consider the potential benefits and costs of thyroid dysfunction testing before and during pregnancy. There is controversy over whether to treat subclinical thyroid dysfunction in pregnant women. This article reviews the most important studies associated with SCH and attempts to draw literature-based conclusions on the management of subclinical hypothyroidism in pregnancy.

Keywords: Subclinical hypothyroidism, pregnancy, screening, levothyroxine treatment.

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INTRODUCTION

Hypothyroidism is the most common pregnancy-related thyroid dysfunction, affecting 3-5% of all pregnant women. Subclinical hypothyroidism (SCH) is more common than overt hypothyroidism and is often described as a serum thyroid-stimulating hormone (TSH) more than the expected than pregnancy specific range at each laboratory level or with a concentration of serum TSH above 2.5 mIU / L in the first trimester and over 3 mIU / L in the second and third trimesters [1]. Hypothyroidism refers to a lack of thyroid hormone production and can be a primary abnormality of the thyroid gland, secondary or central (due to hypothalamic or pituitary). The term 'subclinical hypothyroidism' is used to describe that stage of primary hypothyroidism where there is a high level of thyroid-stimulating hormone (TSH) in the presence of serum-free thyroxine (T4) and triiodothyronine (T3) [2].

This review addresses the below aspects

- Definition of subclinical thyroid disease
- Prevalence of subclinical thyroid disease
- Possible adverse outcomes associated with SCH in pregnancy
- Isolated hypothyroxinaemia and pregnancy and do they need treatment?

- Overt Hypothyroidism and pregnancy
- Adverse outcomes associated with Hypothyroidism in pregnancy
- Does women in reproductive age group need screening for Thyroid peroxidase (TPO) antibodies before or during pregnancy

Definition of subclinical thyroid disease

Subclinical hypothyroidism (SCH) is defined as a level of serum thyroid-stimulating hormone (TSH) above the normal range despite normal levels of serum-free thyroxine. Serum TSH has a log-linear relationship with circulating thyroid hormone levels (double conversion to free thyroxine will result in a 100-fold change in TSH). Therefore, serum TSH measurement is a necessary test to detect minor thyroid dysfunction when circulating hormone levels are within the normal laboratory range [1]. Subclinical hypothyroidism or mild thyroid dysfunction is a common complication, the prevalence of 3% to 8% in people without known thyroid disease [2]. The prevalence increases with age and normally higher for women. After sixty years, the increase in males is closer to females, with a combined concentration of 10% [3]. Antithyroid antibodies are found in 80% of patients with SCH, and 80% of patients with SCH have a serum TSH of less than 10 mIU / L [4].

Prevalence of subclinical thyroid disease

SCH is relatively prevalent in the general population, especially women and the elderly. The incidence of SCH range 4- 10% depending on gender, age and ethnicity. SCH consequences vary in several levels and may depend on the degree and level of serum TSH [1].

The prevalence of thyroid disease and SCH in pregnancy has been widely reported to vary with published literature. This variability is due to differences in the diagnostic procedures for euthyroid status, iodine status, nationality and gestational age at test. As a result, the acceptable rate of increase is not present in various thyroid diseases in pregnancy. A better understanding of the true increase has important implications for clinical management and ongoing discussion regarding universal testing [5].

There is no consensus on the impact of SCH on pregnant women in literature or major guidelines. The prevalence of SCH in pregnancy is estimated to be 2-3 percentages [6]. According to Night and colleagues, the increase in SCH in a Caucasian woman is reported to be just under 14%. The prevalence of SCH in the US ranges from 2 - 2.5% [7]. In Belgium, the prevalence of SCH reported 6.8%, reaching 13.7% in Spain [8]. A multicentre study in India reported that just over 13% of pregnant women had hypothyroidism. Most of these cases were in the subclinical range and reported in the first trimester of pregnancy. The prevalence of hypothyroidism and subclinical hypothyroidism during pregnancy is estimated to be 0.3-0.5% and 2-3%, respectively. In about 5-18% of women of reproductive age, thyroid autoantibodies are present [6].

Consequences of untreated subclinical thyroid disease and do they warrant screening

Thyroid hormones are essential for normal development of the foetus, especially during the first 3 months. Maternal hypothyroidism during the antenatal period is associated with complications. Therefore, screening for thyroid problems should be done in early pregnancy. It will help to diagnose cases early and make timely interventions to prevent negative post-natal effects.

American College of Obstetricians and Gynaecology (ACOG) guideline in 2015 recommends thyroid tests only for pregnant women who are at high risk, symptomatic or have a history of thyroid disease, Type 1 DM or other immune disorders [9].

Symptoms of SCH, even if existing ones, are often subtle, and patients often say that their symptoms are due to their pregnancy. Understandably, even with severe overt hypothyroidism (OH) during pregnancy, the symptoms can vary greatly. According to Canaris et al., overt hypothyroidism was more likely to report symptoms of hypothyroidism than people with

euthyroid but 30% of OH patients had symptoms and 17% of controls reported symptoms of hypothyroidism [10]. Approximately 20% of patients with hypothyroidism did not report symptoms, so the absence of any symptoms failed to rule out OH or SCH.

At least in few of observational studies, SCH in pregnancy has been associated with adverse maternal complications including abnormal placenta, miscarriage, retained products post-delivery, low birth weight, eclampsia and pre-eclampsia [1-5], but some other studies have not found any adverse postnatal effects in SCH [9, 10].

Screening for subclinical hypothyroidism

Screening tests are always been a controversial area between the various guideline groups due to non-consensus between physician groups. For example, while the American Thyroid Association (ATA) recommends screening all adult women over the age of 35 years every five years [11]. RCP believes it is baseless for the general public but acknowledges that exceptions should be made to the various risk groups [12]. The panel recommended against the screening of all pregnant women but argued for the screening cases in certain high-risk groups as mentioned in the US Preventive Service Task Force [10]. The panel believed that special consideration should be given to pregnant women, but only if they are at high risk for thyroid disease (Eg: personal and or family history of thyroid disease or autoimmune disease). Regular screening check-ups for pregnant women recommended by AACE [11] The controversy also remains with regards to the best screening test for SCH in this situation, TSH or T4 [6].

Possible complications associated with SCH in pregnancy

SCH is associated with an increased risk of adverse pregnancy complications and possibly an increased risk of neurological deficits of the foetus. Compared to OH, which has shown more complications, however, SCH-related data vary. In one of the much-quoted study, Negro and colleagues [13] published data suggesting that SCH increases the risk of female pregnancy complications if they have anti-thyroid peroxidase antibody-positive (TPO Ab). A prospective randomized trial of 4000 women, who were categorised as low risk, tested positive in early pregnancy for Thyroid peroxidase and TSH level > 2.5 mIU / L were reviewed. With this combination, levothyroxine treatment started with an aim of normalisation of TSH level. In a control cohort of similar size pregnant women were seen and followed up from early pregnancy, but serum TSH and TPO Ab concentrations analysis was delayed until postpartum, so no thyroxine was given to this group. This allowed the head to head comparison of the effects of thyroxine administration on women who were TPO Ab and had TSH values above 2.5 mIU / L and those found in

untreated controls. The results confirmed a significant reduction in pregnancy complications in the treated group. In a subsequent analysis of the same data, Negro and colleagues [7] reported the highest miscarriage rate for TPO Ab positive women with TSH levels between 2.5 and 5.0 mIU / L compared with those with TSH levels below 2.5 mIU / L (6.1% vs. 3.6% respectively). The latter study had no interventional component. This study was supported by previously published research done by Casey and colleagues [14]. In that study, an increased risk of 2-3 times pregnancy complications was noted in untreated women with SCH. Similarly, Benhadi and his team [15] conducted a case-control study investigating the risk of a miscarriage of just under 2500 Dutch women. In this cohort of pregnant women who do not have OH, the risk of miscarriage has increased with higher TSH in pregnancy.

However, some other research data shows contradictory conclusions. Cleary-Goldman and team [16] did not report any adverse effects from subclinical hypothyroidism in pregnant women (diagnosed in the first and second trimesters) in a group of just fewer than 11000 women. However, the study drew its conclusion after only using the small selective cohort of the whole study group (29% of the study group) with the gestational age between the 10.5 and 14th-week pregnancies. Besides, women were only included in the study if their pregnancy continued and a serum sample analysis done in the second trimester. Mannisto [17] analysed the correlation between the outcome of the pregnancy and thyroid function tests obtained at 12-week pregnancies of just over 5800 women, from the first group of over 9200 women, and found no adverse effect on chronic mortality. However, as only 63% of the total study subject was included in this analysis (5805/9247), data interpretation was limited.

In a published study on miscarriage, Ashoor and colleagues [18] examined TSH and FT4 levels in over 200 single pregnancies between 11-13 weeks of gestation that resulted in miscarriage or stillbirth and

compared the thyroid function tests with those of 4318 normal pregnancies. Women experiencing miscarriage or foetal loss had elevated TSH levels above 97.5th percentile (5.9% vs. 2.5%, $p < 0.05$) and FT4 levels below 2.5th percentile (5.0% vs. 2.5%, $p < 0.05$). Currently, some high-quality evidence suggests that SCH is associated with an increased risk of pregnancy complications.

The adverse effect of SCH on neurocognitive development of the foetus is less clear. A large case-control study showed a decrease in intelligence quotient (IQ) among children born to untreated women compared to euthyroid controls. Data by Haddow *et al*. [19] explained the IQ deficit of 7 points in the spring of untreated hypothyroid women in addition to motor, language, and attention at 7-9-year-old age. Similar retrospective data were previously published by Man and team [20], although such older data must identify patients based on serum butanol- iodine extract in contrast to the thyroid function level. Data from experiments controlled by the Controlled Antenatal Thyroid Screening, presented at the International Thyroid Congress in 2010, challenged this analysis. The main results of this study were the IQ of 3.5-year-old children and the percentage of children with IQ <85 in 3.5-year-old among children whose mothers were treated for SCH and/or hypothyroxinaemia compared with children whose mothers had not been treated. For therapeutic purposes, the analysis was no different from any of these results. In the second conclusion, which included an analysis based on completing the study, there was no difference in IQ claims. However, the percentage of children with IQs <85 was higher in the untreated group compared with the treated group (15.6% vs. 9.2%, $p = 0.009$). The data presented at the International Thyroid Congress did not affect the findings based on whether these women had SCH or special hypothyroxinaemia. In summary, the association between maternal SCH and foetal neurocognitive abnormalities can occur [21], albeit poorly represented (Table 1).

Table-1: Studies of Subclinical Hypothyroidism and maternal outcome

Author	TFTs (Done Mean/Median wks)	Definition of SCH (TSH value in mU/L)	Outcome	Adjusted analysis	Finding	Comments
Casey <i>et al</i> . N = 17,298	Less than 20 wks	TSH (2.74–5.09 mU/L; gestational age specific)	Perinatal outcomes	No	Preterm delivery: unadjusted RR 1.8 [1.1–2.9] Abruptio: unadjusted RR 3.3 [1.1–8.2]	
Cleary-Goldman <i>et al</i> . N = 10,990	Taken (1st and 2nd trimesters)	TSH (1st 4.28 mU/L; 2nd 3.93 mU/L)	Perinatal outcomes	Yes	No association	
Benhadi <i>et al</i> . N = 2497	13 weeks until end 2nd trimester	TSH >5.6 mU/L	Pregnancy loss	Yes	OR 1.8 [1.07–3.03] per TSH doubling	Small number of subjects in the high TSH cohort
Mannisto <i>et al</i> . N = 5805	Mean 10 wks until less than 20 weeks	TSH (3.6 mU/L)	Perinatal outcomes	No	No association	Analysis of only 5808 out of 9247 subjects TPOAb and Tg Ab associated with perinatal mortality,

						after adjustment for age and parity TPOAb RR 3.2 [1.5–7.1]
Negro <i>et al.</i> N = 4123	Less than 11 wks	TSH 2.5–5.0 mU/L	Pregnancy loss Preterm delivery	No multivariate analysis; adjusted only for smoking	Pregnancy loss OR 1.16/mIU [1.00–1.34] Preterm delivery: no association	Study inclusive of only TPOAb-negative women
Mannisto <i>et al.</i> N = 5,805	11 wks	TSH (3.6 mU/L)	Pregnancy complications	Yes	No association	Study primarily focused on endpoints of preeclampsia and gestational diabetes
Sahu <i>et al.</i> N = 633	Between 13 to 26 wks	TSH >5.5 mU/L (not pregnancy and trimester specific)	Pregnancy and perinatal complications	No	Cesarean section rate for fetal distress: OR 2.8 [1.2–6.6] ($p = 0.04$)	
Su <i>et al.</i> N = 1017	Upto 20 wks	3.77–4.35 mU/L; (gestational age specific)	Pregnancy, perinatal and child development outcomes	Yes	Fetal distress: OR 3.65 [1.44–9.26] Preterm delivery: OR 3.32 [1.22–9.05], Poor vision development OR 5.34 [1.09–26.16] Neurodevelopmental delay OR 10.49 [1.01–119.19]	No data on TPOAb status. Small numbers of affected individuals leading to low power for statistical analysis
Karakosta <i>et al.</i> N = 1170	14 wks	TSH Trimester specific (1st >2.53 mU/L; 2nd >2.73 mU/L)	GDM and perinatal outcomes	Yes	Low birth weight, RR 3.1 [1.2–8] GDM (only if TPOAb positive), RR 4.3 [2.1–8.9]	
Lazarus <i>et al.</i> N = 21,846	12 wks	TSH Variable in time (UK >3.65 mU/L; Italy >3.50 mU/L)	Child IQ	N/A	No association	
Korevaar <i>et al.</i> N = 5971	13.2 wks	TSH (>4.04 mU/L)	Premature delivery	Yes	OR 1.87 (1.11–1.34)	Not significant finding after exclusion of TPOAb-positive subjects
Ong <i>et al.</i> N = 2411	11.1 wks	TSH (TSH >2.15 mU/L)	Pregnancy and fetal outcomes	Yes	No association	
Chen <i>et al.</i> N = 8012	14% 1st trimester, 33% 2nd trimester, 53% 3rd trimester	TSH Trimester specific (1st >3.47 mU/L; 2nd >3.81 mU/L; 3rd >4.99 mU/L)	Hypertension, PROM, low birth weight, IUGR	Yes	Hypertension: OR 2.24 [1.25–4.02], PROM: 6.01 [3.98–9.10], IUGR 3.34 [1.75–6.38], and LBW 2.92 [1.65–5.16]	Majority of subjects assessed late in pregnancy (3rd trimester)
Godoy <i>et al.</i> N = 5646	Median 13.2 weeks	TSH (TSH >4.04 mU/L)	Childhood growth, body composition and cardiovascular characteristics.	Yes	No association	
Medici <i>et al.</i> N = 5153	13.5 weeks	TSH (TSH >4.04 mU/L)	Blood pressure and hypertensive disorders	Yes	No association	
Liu <i>et al.</i> N = 3147	4–8 weeks	TSH (TSH 5.22)	Miscarriage	Yes	Increased risk for women when TSH >5.22 (OR 3.4 [1.6–7.2]), or women with thyroid autoimmunity (OR 2.7 [1.4–5.1]). Synergistic worsening when both SCH and autoimmunity together.	Thyroid autoimmunity defined as either TPOAb or TgAb positivity
Leon <i>et al.</i> N = 2170	Mean 13.5 weeks	TSH (TSH >3.5 mU/L)	Pregnancy and fetal outcomes	Yes	No association	No analysis of subclinical hypothyroidism
Kumru <i>et al.</i> N = 497	10–12 weeks	TSH (TSH level not reported)	Pregnancy and perinatal outcomes	Yes	Preterm delivery: OR 4.8 [1.89–12.42] No association with other maternal or perinatal outcomes.	Synergistic effect of thyroid hormone status and TPOAb status analyzed
Päkkilä <i>et al.</i> N = 5131	Mean 10.5 weeks	TSH >3.1 mU/L in 1st or >3.5 mU/L in 2nd	ADHD	Yes	SCH was not associated with an increase in ADHD symptoms TSH was continuously associated with ADHD symptoms in girls	
Taylor <i>et al.</i> N = 769 (women given thyroxine)	1st trimester	3 endpoints: >2.5, >4.5, >10 mU/L	Miscarriage	Partial	TSH >4.5 associated with an increased risk of miscarriage. Graded effect with increasing TSH	

*SCH-subclinical hypothyroidism; GDM- gestational diabetes mellitus; IUGR- intrauterine growth restriction; PROM-premature rupture of membranes; ADHD-attention deficit hyperactivity disorder; LBW- low birth weight

Isolated hypothyroxinaemia and pregnancy

There has been debate as to whether hypothyroxinemia itself can cause complications on the foetus. Pop and his team [22] reported a decline in psychomotor test scores among children born to women with low FT4 levels. These women used to have normal serum TSH levels. Li and colleagues [23] observed a similar decrease in IQ of babies whose mothers suffered from hypothyroidism or isolated hypothyroxinaemia during the first trimester. There was controversy about the method of these studies as well as the credibility of conclusions. Based on Generation R study, Henrichs and colleagues [24] published prospective, non-invasive study which looked at the development of communication in children born to women with isolated hypothyroxinaemia. A 1.5- to 2-fold increase in the risk of unwanted complications (at 3 years of age) was associated with maternal FT4 at low 5 and 10 percentiles.

Isolated hypothyroxinemia-merit treatment?

To date, no randomized clinical trial of thyroxine was performed on pregnant women with distinct hypothyroxinemia. A recent Controlled Antenatal Thyroid Screening (CATS) study investigated suboptimal gestational thyroid function (SGTF) treatment in childhood comprehension and found no difference in intelligence quotient (IQ) for 3 years among children of SGTF-treated mothers. They measured IQ in the same children as 9.5 years of age and included children from normal mothers of normal pregnancy (normal mothers-GTF).

Hales and colleagues (25) reported that there was no difference in IQ <85 between children of mothers with normal GTF and combined SGTF and untreated (fully adjusted range of complications [OR] = 1.15 [95% confidence interval (CI) 0.52, 2.51]; P = 0.731). Moreover, there was no significant effect of treatment [non-treatment OR = 1.33 (95% CI 0.53, 3.34); treatment OR = 0.75 (95% CI 0.27, 2.06) P = 0.576]. Analyzing the accounting of SGTF-treated women with free thyroxine > 97.5th percentile of the entire CATS-I group showed no significant effect on the IQ <85 of the child in CATS-II. The 3-year-old IQ predicted the 9.5-year-old IQ (P <0.0001) and rated 45% of the variance.

Overt Hypothyroidism and pregnancy

Many retrospective and case-controlled studies have confirmed the negative effects of OH on pregnancy and foetal health. Although no prospective, randomized clinical trial of thyroxine intervention has been performed in OH pregnant women, such a study would not be ethical. The available information confirms the benefits of OH treatment during pregnancy.

OH should be treated during pregnancy. This includes women with TSH levels above the trimester-related index frequency with reduced FT4, and all women with TSH concentration above 10.0 mIU / L regardless of FT4 level.

Euthyroid women and Thyroid antibody positive-do they pose a risk?

In 1994, Glinoeer and colleagues [26] conducted a prospective study in 87 women with euthyroid who had thyroid autoantibody positive before and during early pregnancy. Twenty per cent of the women in the study developed a TSH level of > 4 mIU / L during pregnancy despite normal TSH and no need for levothyroxine before childbirth. This happened despite the expected drop in thyroid antibody degrees during pregnancy. Twelve years later, in a randomized study, showed similar results [13]. The authors found that in women with Thyroid antibody-positive euthyroid, TSH levels increased steadily as the pregnancy progressed, from an average of 1.7 mIU / L (week 12) to 3.5 mIU / L at term, with 19% of them have a normal amount of TSH on delivery. These findings confirmed that the growing demand for thyroid hormone occurs during pregnancy. In women with Thyroid antibody positive, both OH and SCH can occur during pregnancy stress as the thyroid's ability to increase production is impaired, an increased demand outstrips the supply. When this happens, an elevation of serum TSH occurs. In summary, Thyroid Antibody positive patients may have a risk of developing hypothyroidism later in pregnancy because some residual thyroid function may act as a buffer during the first trimester.

Adverse outcomes associated with Overt Hypothyroidism (OH) in pregnancy

Hypothyroidism in pregnancy is associated with an increased risk of adverse pregnancy complications, as well as adverse effects on cognitive and fetal brain development [19]. Certain side effects associated with maternal OH include increased risk of premature birth, low birth weight, and miscarriage. Abalovich *et al.* [27] has shown that these patients carry an estimated 60% risk of foetal loss when OH is not detected and adequately treated. Leung *et al.* [28] showed a 22% risk of developing high blood pressure in pregnant women with OH, which is higher compared to euthyroid women or those with SCH. Allan and colleagues [7] also described an increased risk of infant mortality among pregnant women with OH. In conclusion, a strong association between OH and adverse risk factors in the maternal component has been shown.

Table-2: Thyroid Peroxidase Antibody Positivity and Adverse Maternal Outcomes

	TFTs (Mean weeks)	Outcome	Adjusted analysis	Association with antibodies	Additive effects SCH	Comments
Cleary-Goldman N = 10,990	1st and 2nd trimester (test done twice)	Perinatal outcomes	Yes	TPOAb positivity associated with PROM (OR 2.4–3.1)	Not investigated	
Benhadi N = 2497	13 weeks to end of 2nd trimester	Pregnancy loss	Yes	TPOAb positivity not associated with miscarriage.		Adjustment for TSH did not change significant continuous association for TSH. Absolute risk very low
Mannisto N = 5805	10 weeks to 20 weeks	Perinatal outcomes	No	If TgAb positive, a larger proportion of noncephalic presentation at birth (3.6 vs. 6.3%), as well as perinatal mortality (0.8 vs. 1.2%) If TPOAb positive, larger proportion of LGA (5.0 vs. 2.4%) and perinatal mortality (2.4 vs. 0.8%)	Not investigated	
Karakosta. N = 1170	14 weeks	Gestational Diabetes and perinatal outcomes	Yes	OR 1.7 for spontaneous preterm delivery.	TAI + TSH >97.5%: OR 4.3 for GDM TAI + TSH >97.5%: OR 3.1–3.7 for LBW	Thyroid autoimmunity defined as positive TPOAb and/or TgAb
Korevaar N = 5971	13.2 weeks	Premature delivery	Yes	TPO pos. + TSH >97.5%: OR 2.53 TPO pos. + TSH >2.5 mU/L: OR 2.18 TPO pos. + TSH >2mU/L: OR 1.75 (ns) TPO pos. + TSH >median: OR 1.4 (ns)		
Medici N = 5153	13.5 wks	Blood pressure and hypertensive disorders	Yes	No association for TPO Ab pos.		
Liu. N = 3147	4–8 wks	Pregnancy loss	Yes	Thyroid autoimmunity alone OR 2.71 TAI with TSH 2.5–5.22: OR 4.96 TAI with TSH >5.22: OR 9.56		TAI defined as positive TPOAb and/or TgAb with normal TSH and FT4
Päkkilä N = 5131	10.5 wks	ADHD symptoms	Yes	TPO Ab positivity not associated with ADHD symptoms	Not investigated	Exclusion of TPOAb-positive women did not change the results

The investigations that have looked at the association between elevated maternal TSH concentration and adverse clinical endpoints can be grouped into three categories below based upon adverse endpoints. These include adverse effects on pregnancy outcome (i.e., pregnancy loss), adverse perinatal outcomes (i.e., premature delivery, hypertensive disorders), and adverse neurocognitive outcomes (IQ) in offspring.

Should women need to be tested for TPO antibodies before or during pregnancy?

Negro and colleagues [8] reported a potential, randomized levothyroxine intervention in euthyroid patients who were Thyroid Peroxidase Antibody Positive. They reported a decrease in miscarriage rate in the treated group when compared to control group (3.5% vs. 13.8%, $p < .05$). The study limit was that the first gestational age for thyroxine treatment was 10

weeks of gestation, and nearly all of the miscarriage occurred at less than 11 weeks except 1.

There is little evidence to recommend for the screening of all women for thyroid antibody in the first trimester of pregnancy.

CONCLUSION

Over the past few years, significant progress has been made in measuring the physiological changes that occur in pregnancy and the impact of subclinical hypothyroidism on pregnancy and abdominal outcomes. Hypothyroidism is present in 2-15% of pregnant women. It is mainly caused by iodine deficiency in developing countries and thyroid disease in the developed world. Subclinical hypothyroidism has been linked to many adverse events, including miscarriage, premature delivery, gestational diabetes and decreased neurologic development in the foetus. Pregnant women on thyroxine medications need to be euthyroid during the entire pregnancy. It is well understood that treating excessive hypothyroidism can reduce the complication for mother and child. On the other hand, the available evidence to treat subclinical hypothyroidism is limited and contradictory. The universal test for all pregnant women with hypothyroidism is also contradictory. Screening for thyroid antibody also not recommended in pregnancy and there is no consensus among different guidelines. There needs to be guidance depending on studies in the treatment of subclinical hypothyroidism during pregnancy.

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