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# CURRENT ISSUES REGARDING HYPOTHYROIDISM IN PREGNANCY

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***Abstract:*** *The impact of hypothyroidism on pregnancy leads to an increased frequency of obstetric maternal and fetal complications. The universal screening for the detection of hypothyroidism in pregnancy remains a controversial topic. This article presents the current issues of hypothyroidism in pregnancy, and certain aspects of diagnosis, treatment, monitoring and screening.*

***Key words:*** *subclinical hypothyroidism, overt hypothyroidism, universal screening of thyroid.*

## 1. Introduction

During pregnancy there is a slight increase in volume of the thyroid gland due to glandular hyperplasia and increased vascularization. Serum levels of TSH and TRH remain unchanged, while the TBG (thyroxin - binding globulin) increases due to estrogen stimulation. The level of TBG that is increasing is associated with a significant increase in total triiodothyronine (T3) and thyroxine (T4), without any change of the free fractions [8].

The delivery of maternal placental thyroid hormone is necessary for normal fetal development and in particular for the intellectual development. Although fetal thyroid starts to function at 10-12 weeks of gestation, the synthesis of the thyroid hormone occurs only at 18-20 weeks of gestation, so that by this time the fetus is totally dependent on maternal thyroid hormones [5].

## 2. Levels of TSH and FT4

Normal levels of TSH and FT4 are shown in Table 1. [3], [16]

*Normal levels of TSH and FT4* Table 1

| | TSH (mUI/L) | FT4 (pmol/l) |
|---|---|---|
| **Outside pregnancy** | 0.4-4 | 11-23 |
| **Pregnancy – 1st Trimester** | 0.1-2.5 | 11-22 |
| **Pregnancy – 2nd Trimester** | 0.2-3 | 11-19 |
| **Pregnancy – 3rd Trimester** | 0.3-3 | 7-15 |

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Hypothyroidism during pregnancy is defined by the presence of elevated levels of TSH. Dosage of FT4 is required to classify the overt or subclinical hypothyroidism and also for the detection of hipothyroxinemia. Laboratory diagnosis of subclinical and overt hypothyroidism, as for hipothyroxinemia is shown in Table 2 [16].

The most common cause of hypothyroidism during pregnancy, when there it exists sufficient intake of iodine is the autoimmune thyroiditis (Hashimoto), translated by the presence of anti-thyroid antibodies [6].

The influence of pregnancy on hypothyroidism is usually negative. This happens because the maternal thyroid gland should produce a greater amount of hormones during pregnancy, and women with hypothyroidism are less able to support this production. In case of patients with subclinical hypothyroidism, it is observed a reduced functional thyroid reserve, so that, usually hypothyroidism develops or worsens as the pregnancy progresses [6].

Table 2

*TSH and FT4 laboratory values in different affections*

| | TSH | FT4 |
|---|---|---|
| **Subclinical hypothyroidism** | 2.5-10 mUI/L | Normal |
| **Overt hypothyroidism** | >2.5 mUI/L | Decreased |
| | >10 mUI/L | Indifferent |
| **Hipothyroxinemia** | Normal | Decreased |

Pregnant women with hypothyroidism have a higher risk of obstetrical complications: miscarriage, anemia, gestational hypertension, abruption placenta, postpartum hemorrhage. The risk of these complications is higher in women with overt hypothyroidism than in case of subclinical hypothyroidism. Untreated maternal hypothyroidism can lead to premature birth, fetal low birth weight, and neonatal respiratory distress. Recent studies provide sufficient evidence on the role of thyroxin in the development of the normal brain of the fetus, its deficit being translated into a low IQ than the children born from healthy or treated mothers [13].

The treatment of choice for hypothyroidism is levothyroxine.

## 2. ATA and ESA recommendations

The recommendations of ATA (American Thyroid Association) since 2011 and ESA (Endocrine Society of America) in 2012 on the treatment of hypothyroidism during pregnancy are shown in Table 3 [2], [16].

Table 3

*ATA/ESA recommendations in the treatment of hypothyroidism in pregnancy*

| | **Treatment with levothyroxine** |
|---|---|
| **Overt hypothyroidism** | Yes |
| **Subclinical hypothyroidismAcTPO+** | Yes |
| **Subclinical hypothyroidism AcTPO-** | No – ATA, Yes – ESA |
| **Hipothyroxinemia** | No |

The goal of the treatment is the normalization of the level of TSH and also integration into the reference value specific for each trimester.

Women with subclinical hypothyroidism that are not on treatment for this disease and also women with anti-thyroid antibodies present, must be monitored by testing TSH and FT4 every 4 weeks as far as 16-20 weeks of gestation and also , at least once between 26-32 weeks of gestation.

Women with hypothyroidism that are intending to become pregnant should adjust the dose of thyroxine such as TSH levels to be below 2.5 mUI/L. Lower values of TSH before installing pregnancy is associated with a lower risk of increased TSH in the first trimester of pregnancy .

Women who are already being treated for hypothyroidism should increase the dose of thyroxine by 25-30 % immediately after the installation of pregnancy. There is a wide variation regarding the dose of thyroxine required to maintain a normal TSH level in pregnancy, some women requiring an increase in the dosage of 10-20 %, and other need to increase the dose with 80%.

At every 4 weeks in the first half of pregnancy, the monitoring of TSH should be performed because many adjustments in the levothyroxine dose are often required. It is also recommended monitoring the level of TSH at least once between weeks 26-32 of gestation.

After birth, the levothyroxine dose should be reduced to the original dose before pregnancy and TSH testing should be performed at 6 weeks postpartum.

## 4. Discussions

The questions on making screening to all pregnant women with the purpose of observing a possible thyroid dysfunction or simply selecting high-risk cases have become a controversial topic in the recent years [4], [7], [10], [12], [15].

Recent studies have clearly marked the maternal and fetal adverse effects associated with undiagnosed or untreated thyroid dysfunction.

*Cases with high risk of hypothyroidism according to ATA/ESA* Table 4

| High risk | ATA | ESA |
|---|---|---|
| **Age> 30 years** | √ | √ |
| **Family history of thyroid dysfunctions** | √ | √ |
| **Suggestive signs of hypothyroidism** | √ | √ |
| **Clinical goiter present** | √ | √ |
| **Antithyroid antibodies positivity** | √ | √ |
| **Type I diabetes , autoimmune diseases** | √ | √ |
| **Infertility** | √ | √ |
| **History of preterm delivery / repeated miscarriages** | √ | √ |
| **History of pathology / surgery on thyroid** | √ | √ |
| **History of irradiation of the head / neck** | √ | √ |
| **Patients from regions with iodine deficiency** | √ | √ |
| **Morbid obesity (BMI > 40kg / m²)** | √ | |
| **Treatment with amiodarone, lithium** | √ | |

Although TSH determination is accessible and not expensive, there is insufficient evidence favouring performing screening for detection of thyroid dysfunction. So that, in 2011, the ATA guidelines indicates that universal screening is not recommended to be performed [16].

ATA recommendations are not universally accepted. ESA Committee could not reach a mutual agreement on universal screening, some of the members opined in favour of dosage of TSH at the first visit or at 9 weeks of gestation, while other members thought that thyroid screening should not be performed , but these members support an aggressive case-finding to identify ant treat the high-risk patients. [2]

ATA and ESA believes that the following conditions are correlated with an increased risk for developing hypothyroidism and in those cases is required the TSH assays (Table 4) [2], [16]. The debate on the advantages and disadvantages of universal thyroid screening in pregnancy are ongoing [14].

Currently, a prospective, randomized study, "Controlled Antenatal Thyroid Screening Study" (CATS) is ongoing and is conducted to test the value of thyroid screening in pregnancy [1], [9].

Although there are convincing studies showing that the presence of anti-thyroid antibodies in pregnancy can lead to miscarriage and premature birth, even in the presence of euthyroidism, both ATA and ESA does not recommend universal screening test for anti-thyroid antibodies.

## 5. Conclusions

Most of the times, hypothyroidism develops or worsens as the pregnancy progresses and women with hypothyroidism have a higher risk of obstetric complications.

Treatment with levothyroxine is recommended in overt hypothyroidism and in subclinical hypothyroidism with anti-thyroid antibodies present, and the dosage should be adjusted so that the amount of

TSH fit into the reference values specific for each trimester of pregnancy.

TSH/FT4 monitoring should be performed at every 4 weeks in the first half of pregnancy and also at least once between 26-32 weeks of gestation. It is also recommended to test TSH/FT4 at 6 weeks postpartum.

Universal thyroid screening is controversial. ATA and ESA organizations do not recommend the universal thyroid screening, encouraging only the selected high risk cases.

Further studies are needed to examine the cost-effectiveness of thyroid screening in pregnancy and studies to assess the effectiveness of treatment with levothyroxine for euthyroid pregnant women with anti-thyroid antibodies present.

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