

Hypothyroidism and Pregnancy

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Thyroid disorders are observed about 4 to 5 times more frequently in women than in men. The child-bearing period being the most affected. Therefore thyroid function abnormalities are frequently encountered in pregnant women.

Regulation of thyroid function in normal pregnancy

Hormonal changes and metabolic demands during pregnancy result in profound alteration in the biochemical parameters of thyroid function. These include rise in T4 binding concentration, alteration in the requirement for iodine, and modifications in the autoimmune regulation. The role of placenta in the deiodination of iodothyronine is known. The thyroid hormones are transported bound to thyroid binding globulin and transthyretin. There is a 2.5 fold increase in serum thyroid binding globulin (TBG) in pregnancy which reaches a plateau around midgestation, thereafter remaining unchanged until term. The total thyroid hormones increase in serum which is a direct consequence of increase in serum TBG. These modifications represent the necessary adjustments required from preconception to gestational equilibrium of thyroid economy. In healthy pregnant women these changes are relatively minor and unnoticeable. However, in women with iodine deficiency or autoimmune thyroiditis the thyroid stimulating hormone (TSH) surge is amplified.

HYPOTHYROIDISM AND PREGNANCY

Fertility and pregnancy outcome in hypothyroid women

There is a known association between hypothyroidism and decreased fertility, which is mostly due to ovulatory disturbance. Women requiring treatment with thyroid hormone have a 2-fold risk of primary ovulatory infertility. Observations in the human species are confirmed by animal investigations showing an association between experimentally induced hypothyroidism and menstrual cycle dysfunction.

Hypothyroid women who become pregnant also carry an increased risk for obstetrical complications such as IUD, pregnancy – induced hypertension, abruptio placenta and increase in perinatal mortality. There are indications that thyroid hormone administration greatly improves, although it does not entirely suppress, the frequency of these abnormalities. In general, infants of hypothyroid mothers appear healthy without evidence of thyroid dysfunction, some studies have indicated a higher perinatal mortality and congenital malfunctions which is not confirmed by other investigators. There is also recent evidence for long – lasting psychoneurological impairment in the progeny.

The most common cause of primary hypothyroidism in young women is chronic autoimmune thyroiditis, which occurs, in both goitrous and atrophic forms. It is not clearly understood whether diminished fecundity and increased risk of poor pregnancy outcome observed in hypothyroid women, result from thyroid insufficiency or reflect a more generalized autoimmune disturbance affecting both conception and fetal development.

Subclinical hypothyroidism in pregnancy

The frequency of established hypothyroidism in pregnancy is not clearly known, but conservative estimates suggest a prevalence of 0.3 – 0.7. Subclinical hypothyroidism has been shown to occur more frequently in pregnant women with Type 1 diabetes, who had normal serum TSH levels before conception (a significant proportion of them display thyroid antibody positively). Klein et. al. carried out a retrospective study on a serum data bank from 2,000 consecutive pregnant women in Maine at 15 – 18 weeks of gestation. The authors showed that 2.5% of all pregnant women had supranormal TSH concentrations with one tenth of them exhibiting overt hypothyroidism. They also found that the

prevalence of positive thyroid antibodies in women with subclinical hypothyroidism was 5 fold more frequent than in control pregnant women.

Women with thyroid hypertrophy before pregnancy presumably have a sufficient functional reserve for the thyroid gland to function adequately before gestation (hence allowing them to become pregnant), but not after establishment of the pregnant state. An argument in favour of this hypothesis, is our observation that, when monitored during the postpartum period, thyroid function reverted to normal despite withdrawal of L-T4.

Euthyroid autoimmune thyroid disorders (AITD) and pregnancy

In a cohort study of pregnant women with mild underlying abnormalities published in 1991, it was noted that women who are euthyroid but carry thyroid antibodies at the onset of pregnancy have an increased risk of developing hypothyroidism during gestation. Pregnant women with asymptomatic AITD carry a significant risk of developing hypothyroidism. Hypothyroidism results from the relative inability of the maternal thyroid gland to adjust to the changes associated with pregnancy. Obstetricians and endocrinologists should monitor all pregnant women with AITD closely and jointly.

AITD and the risk of miscarriage

Stagnaro – Green et. al. And Glinoe et. al. were the first to report a strong correlation between positive thyroid antibodies and the risk of spontaneous miscarriage in women who are euthyroid. These results have since been confirmed by other reports, emphasizing that the risk of miscarriage occurs primarily in the first trimester and that women with a history of consecutive abortion carry an even greater risk. Overall, the data presently available suggest that the relative risk of miscarriage is 2 – 4 fold greater in women with asymptomatic AITD. The presence of thyroid immunity represents risk of miscarriage is thought to result from an abnormal stimulation of the immune system. It is also possible that mild degrees of thyroid insufficiency may explain, in part, the higher rate of fetal wastage.

Thyroid hormone replacement in the hypothyroid pregnant women

In the 1980s, the need for a systematic adjustment of the T4 replacement dose during pregnancy was not recognized, and it was actually stated that women with hypothyroidism rarely required a change in T4 replacement. Newer studies have clearly shown that this is not the case. The possible explanation may be the development of sensitive TSH assays that permit a more precise titration of T4 dosage. Many patients may have been over treated before becoming Pregnant. In 1990, Mandel et. al. retrospectively assessed L - T4 requirements before, during and after pregnancy with the use of sensitive TSH, and showed a decrease in serum free T4, changes that indicated the need for increased doses of L - T4. In 1992, Kaplan reported a retrospective analysis of thyroid hormone requirements in a group of 65 women, who were hypothyroid because of Hashimoto's thyroiditis or thyroid ablation for hyperthyroidism. Serum TSH rose markedly when L - T4 replacement doses were maintained at prepregnancy levels, the free T4 levels also decreased (on an average of 40%) and become subnormal in 13% of the cases. In contrast raising the daily L - T4 dosage by 40 - 100 µg resulted in a reversion of TSH concentrations into the normal range. After childbirth, L - T4 requirements were approximately the same as before pregnancy. An increased L - T4 need is already apparent in the first trimester, concomitant with major changes in the thyroidal economy. Hence, adjustment of L - T4 dosage should be done in the early stages of gestation. Individual increments in L - T4 dosage vary widely (between 10% and >100%) with a median dosage increment of 40-50% over the pregestational replacement requirement. A regular clinical and laboratory follow-up is essential, with periodic determinations of TSH and free T4 concentrations.

Therefore to conclude it cannot be stressed enough the importance of recognizing and treating sub clinical and overt hypothyroidism in pregnant women and in those desirous to become pregnant.