Brief Communication

Importance of Universal screening for thyroid disorders in first trimester of pregnancy

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ABSTRACT

Objective: To determine the importance of screening for Thyriod disorders in the first trimester of pregnancy. **Materials and Methods:** The Study was conducted on 305 patients which were were randomly selected and screened on OPD basis by TSH levels (cut off level 0.10-2.50 mIU/ml). **Results:** In the 305 women screened mean age was 24.46 years, mean gestational age was 9.09 weeks, 89.83% were euthyroid, 9.8%were hypothyroid, 0.32% were hyperthyroid. Incidence of hypothyroidism in high risk population was 20.58% and in normal population was 6.7%. There was significant association of thyroid disorders with high risk factors ($P < 0.001$). In hypothyroid women 46% had adverse perinatal outcomes and 53.33% had normal outcomes. This shows statistically significant association abnormal TSH values with adverse pregnancy outcomes ($P < 0.001$). In abnormal perinatal outcomes 6.2% women had Caesarean section out of them 73.68% were euthyroid, 26.31% were hypothyroid 1.9% had preterm labour, out of them 50% were euthyroid, 50% were hypothyroid. Out of 2.2% spontaneous abortions 28.5% were in euthyroid group while 71.4% were in hypothyroid group. There was 1 term stillbirth in hypothyroid group.This study showed significant association between abnormal thyroid stimulating hormone (TSH) values and adverse perinatal outcomes ($P < 0.001$). **Conclusion:** There is significant correlation between risk factors and hypothyroidism. So high risk screening is mandatory in early pregnancy. But if we screen only high risk population we would miss 4.6% cases which could have been diagnosed and treated earlier. Therefore it is important to screen all pregnant women in the first trimester, it should be made mandatory.

Key words: Hypothyroidism in pregnancy, screening in first trimester, Universal screening

Introduction

The role of the thyroid gland in pregnancy and the impact of thyroid disorders on the course of pregnancy and development of the offspring have drawn a considerable interest in the recent years, both in the medical and in the general society. About 2 and 4% women suffer subclinical or overt-hypothyroidism. A growing body of evidence suggests that subclinical hypothyroidism may be associated with *in vitro* fertilization failure, subfertility, infertility, spontaneous abortion, placental abruption, gestational hypertension, preeclampsia, preterm delivery, postpartum thyroid dysfunction, depression (including postpartum depression), conversion to overt hypothyroidism, and impaired cognitive and psychomotor child development. American Thyroid Association in its recently published guidelines have stated against universal screening of pregnant women for hypothyroidism.[1] There has been a wide geographic variation in prevalence of hypothyroidism during pregnancy. It varies from 2.5% from the West to 11% from India.[2,3] It seems that prevalence of hypothyroidism is more in Asian countries compared to the West.[4] In a recent study by Dhanwal *et al.*,[5] a high prevalence of hypothyroidism (14.3%) was noted. Looking at these data the purpose of the study was to know whether routine screening would prove to be beneficial in our country.

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Materials and Methods

The Study was an out-patient department (OPD) based prospective cohort, observational study in which 305

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women were randomly selected and screened on OPD basis by Thyroid-Stimulating Hormone (TSH) levels (cutoff level 0.10-2.50 mIU/ml) as per recent guidelines. The quantification of TSH was carried out with ADVIA Centaur CP/Chemiluminescence. These women were followed till term and subsequent delivery to study the effect on maternal and perinatal outcome. First trimester pregnant women were included in the study. Known cases of other medical disorders and women who did not give consent for TSH estimation were excluded from the study.

The extreme values as taken cutoffs for the diagnosis of hypothyroidism were TSH >2.50mU/L and hyperthyroidism if TSH <0.10mU/L, the reference values for TSH were 0.1-2.5mIU/l, 0.2-3.0 mIU/l and 0.3-3.0 mIU/l in the first, second, and third trimesters of pregnancy respectively, considering the recent literature.[1,6,7] The statistical difference between variables were compared by Chi-square test (*P* value).

Results

In the study following are the observations made:

The mean age of women was 24.46 years (SD = 2.00). The mean gestational age at time of screening 9.09 weeks. (SD = 4.09) 38.68% of women were of gestational age less than 9 weeks and 61.31% were with gestational age 9–13 weeks. Cut off of 9 weeks was taken to identify those who presented early in first trimester, 55.08% women were nullipara, 31.14% were primipara, 11.47% were para 2, 2.2% women were para 3 and more.

It was seen that 4.9% women were already having symptoms of thyroid diseases (main symptoms seen were weakness, lethargy, loss of appetite, weight gain), 4.2% had history of previous thyroid diseases (which is either hypo or hyperthyroidism), 0.65% women had history of other autoimmune diseases (APLA syndrome) 4.9% women had history of previous caesarean section, 1.6% women had family history of thyroid diseases, 0.3% had history of irradiation, 1.6% had history of medication (Thyroxine for Hypothyroidism). On this screening 89.83% women were euthyroid, 9.8% were hypothyroid, and 0.32% were hyperthyroid. However, the incidence of hypothyroidism in high risk population was 20.58% and in normal population was 6.7% which shows a significant association of thyroid disorders with high risk factors ($P < 0.001$).

In the euthyroid women 7.2% had an adverse perinatal outcome, 92.7% had normal outcomes. In hypothyroid women 46% had adverse perinatal outcomes and 53.33% had normal outcomes. This shows statistically significant association abnormal TSH values with adverse pregnancy outcomes ($P < 0.001$).

Considering the route of Delivery, 88.85% women had normal delivery, out of them 0.36% were hyperthyroid, 5.5% were hypothyroid rest were euthyroid. In abnormal perinatal outcomes 6.2% women had lower segment caesarean section (LSCS) out of them 73.68% were euthyroid and 26.31% were hypothyroid. The main indications for LSCS in these cases were fetal distress, maternal Cephalopelvic Disproportion (CPD), contracted pelvis, and failed induction.

1.9% had preterm labour, out of them 50% were euthyroid, 50% were hypothyroid. In all, there was only one preterm fresh still birth in a euthyroid woman.

Out of 2.2% spontaneous abortions 28.5% were in euthyroid group while 71.4% were in hypothyroid group. There was one term fresh still birth in hypothyroid group.

This study shows significant association between abnormal TSH values and adverse perinatal outcomes ($P < 0.001$).

Discussion

This prospective screening of thyroid function in a cohort of unselected pregnant women shows that high-risk women (with a personal or family history of thyroid disorders or a personal history of other autoimmune diseases) have more significant ($P < 0.001$) increased risk of hypothyroidism (subclinical or overt) during early pregnancy. However, testing only the high-risk pregnant women, as the consensus guidelines recommend[8], would miss about one-of women with hypothyroidism. Subclinical hypothyroidism during early pregnancy is common, affecting about 2.5% pregnant women.[9,10] Therefore with the growing evidence for an association between maternal subclinical hypothyroidism and adverse pregnancy outcomes but lack of intervention trials showing beneficial effect of thyroxine (T4) in preventing these adverse outcomes, the controversy between targeted high-risk case finding and universal screening continues.[11-13] The consensus guidelines recommend the use of T4 in pregnant women with subclinical hypothyroidism, justified on the basis of potential benefit to risk ratio.[8] Our study shows that, without universal screening, a significant number of such pregnant women with thyroid dysfunction will not be picked up. Several factors affect thyroid function tests during various stages of pregnancy. Free thyroxine (FT4) increases with suppression of TSH in response to placental human chorionic gonadotrophin during the first trimester, whereas

FT4 tends to decrease in late gestation.[14] This is likely to be the cause for the high prevalence of suppressed TSH in this cohort. Furthermore increased serum thyroid-binding globulin and decreased albumin during pregnancy result in assay-dependent variations in FT4 levels.[15] These observations have led to the call for using trimester and assay-specific reference ranges for thyroid function tests in pregnancy.[16,17] If the trimester specific reference range is used, 9.8% pregnant women in this cohort will be considered to have hypothyroidism. Whereas there will be less of a controversy to use the trimester-specific reference range in titrating the dose of T4 in pregnant women on T4 replacement, further studies are needed to determine the threshold level of TSH at which initiation of T4 replacement should be considered. Clinical studies have confirmed that the increased requirement for T4 (or exogenous LT4) occurs as early as 4-6 weeks of pregnancy.[18] Such requirements gradually increase through 16-20 weeks of pregnancy, and thereafter plateau until time of delivery. These data provide the basis for recommending adjustments to thyroid hormone in affected women once pregnant and for the timing of follow-up intervals for TSH in treated patients.

The levothyroxine (LT4) adjustment, when necessary, should be made as soon as possible after pregnancy is confirmed to reduce the probability of hypothyroidism. Normalization of TSH levels throughout gestation is the goal. A prospective, randomized study has recently provided evidence in support of one dose adjustment strategy for women receiving LT4 who are newly pregnant.[19] For women who are euthyroid while receiving once-daily dosing of LT4 (regardless of amount), a recommendation to increase by two additional tablets weekly (nine tablets per week instead of seven tablets per week; 29% increase) can effectively prevent maternal hypothyroidism during the first trimester and mimic gestational physiology. This augmented dose should occur immediately after a missed menstrual cycle or suspected pregnancy occurs. Confirmatory biochemical testing should also occur simultaneously. A separate option is to increase the dosage of daily LT4 by approximately 25-30%.

There is also an uncertainty regarding the most appropriate initial screening test for thyroid dysfunction in pregnancy. The consensus guidelines recommend using TSH as the initial test[6], whereas others have stressed the importance of testing FT4 by highlighting the fact that FT4 (and FT3) is responsible for thyroid hormone action and that maternal hypothyroxinemia (normal TSH but low FT4) is associated with neuropsychological deficit in the offspring.[18] In our study, 9.8% of pregnant women had hypothyroxemia. The cause of maternal hypothyroxemia is not fully understood, but iodine deficiency is thought to be a major factor although urinary iodine was not analyzed in the present cohort, a previous study in this same population has shown that 7 and 40% pregnant women have urinary iodine excretion of less than 50 g/L (suggestive of dietary iodine deficiency) and 50-100 g/L (suggestive of borderline iodine deficiency).

Nearly one-quarter of hypothyroid women on T4 replacement in this study had raised TSH at their first antenatal visit. Given the fact that the fetus relies entirely on maternal thyroid hormones for its development until about 13 week of gestation, it is critical to ensure adequate T4 replacement in pregnant women during the first trimester. Hypothyroid pregnant women on T4 require an increased dose from as early as the fifth week of gestation to maintain optimum T4 replacement. Some recommend a 30% increase in the T4 dose as soon as the pregnancy is confirmed, with further dose adjustments based on TSH measurements. In addition, through education of all hypothyroid women in the reproductive age, every attempt should be made to ensure an adequate T4 replacement before a planned pregnancy.

Conclusion

Maternal subclinical hypothyroidism during pregnancy is associated with various adverse outcomes. So screening of thyroid disorders should be done in early pregnancy. It will help to diagnose the cases at the earliest and to carry out timely intervention to prevent adverse perinatal outcomes. But still there is a controversy regarding universal thyroid function screening or high-risk screening in early pregnancy. This study shows that there is significant correlation between risk factors and hypothyroidism. So high risk screening is mandatory in early pregnancy. But if we screen only high risk population we would miss 4.6% cases which could have been diagnosed and treated earlier.

So this study emphasizes high risk screening in early pregnancy but also supports that universal screening should be a part of our screening protocols so that all thyroid disorders are screened and treated at the earliest. Even small percentage of thyroid disorders in early pregnancy should not be missed. So in our country we must follow Indian Thyroid Society Guidelines[7] which clearly recommend that "all pregnant women should be screened at 1st antenatal visit by measuring TSH levels", and highlight that"ideally screening should be carried out during prepregnancy evaluation or as soon as pregnancy is confirmed."

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