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ORIGINAL ARTICLE

Screening for Thyroid Dysfunction in 1st Trimester of Pregnancy

[1]Kavitha Karthikeyan, [2]Prabha Swaminathan, [3]Amrita Priscilla Nalini, [4]Bharath Ramji, [5]Annie Thatheus

ABSTRACT

This study was done to find the prevalence of newly diagnosed thyroid dysfunction in early pregnancy in patients attending the antenatal clinic and to emphasize the need for routine screening for thyroid dysfunction in pregnancy. Free thyroxine (FT4) and thyroid stimulating hormone (TSH) levels were measured and cut-off levels set at FT4 0.86–1.86 ng/dl, TSH 0.1–2.5 mIU/l in 1st trimester, TSH 0.1–3 mIU/l in 2nd and 3rd trimesters. A total of 956 pregnant women were screened in 1st trimester after excluding patients with known thyroid dysfunction. About 13.2% were diagnosed as hypothyroid and 1.6% as hyperthyroid. Incidence in high-risk patients was 21.7% and in low-risk was 10.4%. High-risk factors have a strong association for hypothyroidism ($p < 0.001$). Screening only high-risk patients will miss a significant number of patients seen positive in the low-risk group. Hence, it is essential to do routine screening for thyroid dysfunction in pregnancy.

Keywords: First trimester screening, Screening in pregnancy, Subclinical hypothyroidism.

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INTRODUCTION

The influence of thyroid dysfunction in affecting perinatal outcome is well proven. Overt maternal hypothyroidism can lead to congenital cardiac defects, impairment of fetal neuronal differentiation, and development of mental retardation in childhood. Moderately low levels of thyroid hormone in mother can lead to lower IQ levels in children. Other complications associated with subclinical hypothyroidism are spontaneous abortions, placental abruption, preterm labor, gestational hypertension, postpartum depression, and development of overt hypothyroidism in future. This can be overcome by diagnosing hypothyroidism early in first trimester and thyroxine supplementation. Screening only low-risk women could miss 30% of overt and subclinical hypothyroid patients who will benefit from treatment.[1] The prevalence of hypothyroidism is quite high, about 11% in India compared to 2.5% in the West.[2]

Patients with uncontrolled hyperthyroidism have an increased risk of miscarriage, abruption placenta, pre-eclampsia, and preterm labor, low-birth-weight babies, fetal and neonatal hyperthyroidism.[3] Subclinical hyperthyroidism is more often gestational, is transient, and requires only monitoring. It is not associated with any adverse outcome. The aim of this study is to find out the incidence of newly diagnosed patients with thyroid dysfunction by antenatal screening in first trimester and to emphasize the significance of routine screening.

MATERIALS AND METHODS

The study was a prospective observational study in all pregnant women in first trimester who attended the antenatal clinic in Chettinad Hospital and Research Institute (CHRI) over a period of 1.5 years from May 2013 to November 2014. Pregnant mothers with known thyroid dysfunction with or without treatment and patients with multiple pregnancies were excluded from the study. A total of 956 patients in first trimester satisfying inclusion criteria were included for the study. After a proper history and examination, the patients are classified as high risk and low risk depending on family history, symptoms and signs of thyroid dysfunction, presence of goiter, and previous obstetric outcome. Thyroid stimulating hormon levels and free T4 were checked by CLIA method along with other booking investigations for all patients irrespective of the risk factors. Cut-off levels for TSH was placed at 0.1–2.5 mIU/mL in 1st trimester and 0.1–3 mIU/l in 2nd and 3rd trimesters and free T4 at 0.86–1.86 ng/dl. The mean age of the patient, gestational age at the time of blood sampling, parity, and presence of high-risk factors were all noted. The diagnosis of overt and subclinical

[1]Assistant Professor, [2]Associate Professor, [3]Professor, [4]Senior Consultant, [5]Junior Resident

[1-3,5]Department of Obstetrics and Gynaecology, Chettinad Hospital and Research Institute, Tamil Nadu, India

[4]Department of Endocrinology, Arka Centre for Hormonal Health Tamil Nadu, India

Corresponding Author: Kavitha Karthikeyan, Assistant Professor, Department of Obstetrics and Gynaecology Chettinad Hospital and Research Institute, Tamil Nadu, India Phone: +91444741000, e-mail: kavikarthik16@gmail.com

hypo- and hyperthyroidism was made accordingly. The number of patients who were diagnosed with hypothyroidism in the low-risk and high-risk groups was noted. After diagnosis, these patients are started on Levothyroxine replacement after consulting endocrinologist; their doses were adjusted according to TSH levels monitored once in 2 months. Statistical analysis from the obtained data is done using Students t test and chi-square test.

RESULTS

Total number of patients studied was 956. Patients were in the mean age of 22.34 years. The mean gestational age of testing was 8.2 weeks. In total, 596 (62.4%) were primiparous, the rest were multiparous. The total number of high-risk patients was 273 (25.8%) and low-risk patients was 683 (71.4%).

Patients with TSH > 2.5 mIU/l were 126, incidence of hypothyroidism was 13.2%. Thirty-six patients (3.8%) had overt hypothyroidism, with low free T4 and increased TSH levels. Ninety patients (9.2%) had subclinical hypothyroidism with normal free T4 levels. Patients with symptoms of thyroid disorders were 35 (3.7%), 2 (0.2%) had undergone previous thyroid surgery. Seven (2.56%) patients had pregestational diabetes mellitus. Fifty-five (20.1%) patients had positive family history of thyroid disorders. As many as 132 (13.8%) had either missed abortion or previous bad obstetric history. On examination, 12 (1.2%) patients had goiter. The incidence of subclinical hyperthyroidism with TSH < 0.1 mIU/l was 15 (1.6%). Two patients (0.2%) had overt hyperthyroidism with elevated free T4 levels.

Among the high-risk pregnancy group (n = 273), 56 had hypothyroidism (20.5%). Among low-risk patients (n = 683), 70 had hypothyroidism (10.2%). There was a significant association between hypothyroidism and high-risk pregnancy ($p < 0.001$). Among high-risk hypothyroid patients, 9 (7.14%) had overt hypothyroidism, 37 (21.4%) had subclinical hypothyroidism (total high-risk hypothyroid patients were 56, but if you add overt and subclinical it comes to only 46). Among low-risk group with hypothyroidism (n = 70), 63 (9.2%) had subclinical hypothyroidism and 7 (1%) had overt hypothyroidism. Among patients with hyperthyroidism (n = 17), 3 (17.6%) belonged to high-risk group and 14 (82.3%) belonged to low-risk group (Table 1).

Table 1: Data showing hypothyroid patients

Total no. of patients n = 956	*High risk groups n = 273*	*Low risk groups n = 683*
Hypothyroid patients n = 126	56 (20.5%)	70 (10.2%)
Overt hypothyroidism n = 36	29 (10.6%)	7 (1%)
Subclinical hypothyroidism n = 90	27 (9.9%)	63 (9.2%)

DISCUSSION

Prevalence of hypothyroidism in Asian population ranges between 11 and 20%. A study by Danwal[4] shows 14.3% in north India, while it is 13.2% in our study. It is quite high compared to the West, where it is about 2.5%,[2] hence the need for routine screening for all pregnant patients in Asian countries. The incidence is more (21.7%) in high-risk population compared to 10.4% in the low-risk population ACOG 2002 guidelines demonstrated the cost-effectiveness of universal screening for thyroid dysfunction in pregnancy.[5] But a considerable number of patients in the low-risk group had hypothyroidism, which points to the need for routine screening in pregnant patients. Joint guidelines from the American Association of Clinical Endocrinologists and the American Thyroid Association (2012)[6] still do not recommend universal screening for high-risk patients. ACOG 2007 guidelines recommend thyroid testing only in high-risk patients. Proper maturation of fetal CNS is dependent on maternal thyroxine levels, especially in the early period of gestation < 16 weeks. This is before the fetal thyroid gland starts functioning. Patients with hypothyroidism diagnosed in early pregnancy should be supplemented with thyroxine to overcome this and other effects like spontaneous abortion.

The upper limit of TSH is decreased to 2.5 mIU/l in 1st trimester and 3 mIU/l in 2nd and 3rd trimesters. There is a fall in TSH levels in pregnancy because of elevated HCG, stimulating the TSH receptor. Free T4 measurement is not reliable in pregnancy because of elevated TBG. Free T4 index assay is a better substitute as recommended by Endocrine Society guidelines in 2012.[7] The risk for miscarriage and preterm delivery has increased when the cut-off level was kept higher. Recent Endocrine Society guidelines recommend thyroxine replacement in all pregnant women with subclinical hypothyroidism.[7] All these patients should be reviewed after delivery as this is a transient phenomenon and most of them will not need replacement later on. A group of patients with normal TSH levels show positivity for thyroid peroxidase antibodies. Most of them are euthyroid. They have increased risk of developing postpartum thyroiditis.[8] But routine testing for TPO antibody is not cost-effective.

Gestational thyrotoxicosis does not need active treatment. In patients with overt hyperthyroidism, Grave's disease should be ruled out. In patients with uncontrolled hyperthyroidism, there is risk of congestive cardiac failure, thyroid crisis, and neonatal thyrotoxicosis.[9]

CONCLUSION

The prevalence of thyroid dysfunction during pregnancy is quite high. Diagnosis of thyroid dysfunction in a

considerable number of low-risk patients points to the need for routine screening for thyroid function in 1st trimester of pregnancy. This will help to reduce perinatal morbidity and adverse outcomes in the offspring when thyroxine supplementation is started early. This study supports that universal screening for thyroid dysfunction should be included in antenatal screening.

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