Journal of Cardiovascular Disease Research
ISSN: 0975-3583, 0976-2833 VOL08, ISSUE 02, 2017

Original Research Article

STUDY ON THYROID DISORDERS IN PREGNANT WOMEN ATTENDING OUR TERITIARY CARE CENTRE

Dr. [1] Lalitha Umesh Srinivas (first and corresponding author), Assistant Professor, Dept. of OBG, Gouri Devi Institute of Medical Sciences & Hospital, Durgapur, WB

ABSTRACT

Aim and Objectives: The aim and objective of the study is to determine the prevalence of thyroid disorders in pregnancy.

Materials and Methods**:** Basic hematological and biochemical investigations were carried out along with thyroid function tests (TSH, FT3, FT4, anti TPO antibody titers). All the patients were subjected to first trimester ultrasound scan to confirm gestational age less than 12 weeks. The reference interval for thyroid panel were as per ATA guidelines. Thyroid profiles were done by the chemiluminescence method. For this study, the trimester-specific upper limit value for TSH was taken as <2.5 mIU/mL for the first trimester and <3 mIU/mL for the second and third trimesters as per American Thyroid Association (ATA) 2011 criteria. Patients with TSH levels higher than the trimester specific level and normal fT4 levels were diagnosed with SCH. Anti-TPO level <60 U/L was taken as normal upper limit as per manufacturer's protocol. Level more than 60U/L is considered a raised anti-TPO titer.

Discussion and Conclusion: Thyroid dysfunction during pregnancy and the postpartum period is a common obstetric problem primarily managed by GPs. At-risk women are screened, but universal thyroid function screening is currently not recommended during pregnancy or postpartum. Thyroxine is used for treating overt hypothyroidism and is recommended in antibody positive subclinical hypothyroidism. For hyperthyroidism, propylthiouracil is the preferred antithyroid drug in the preconception and first trimester to reduce the risk of teratogenicity. Carbimazole may be used in the second trimester. This present study revealed an increase in subclinical hypothyroidism in pregnancy in our population. A significant number of SCH with high anti-TPO antibody titer points towards autoimmunity as being a significant cause of the decreased level of thyroid hormones in pregnancy.

Key-words: pregnancy, euthyroid, hypothyroidism, hyperthyroidism, anti TPO antibodies and thyroid stimulating hormone.

INTRODUCTION:

The incidence of hypothyroidism in pregnancy is higher in Asian countries, with more observed in the Indian population being attributed to nutritional as well as immunological origins. Even subclinical hypothyroidism (SCH) with high thyroid-stimulating hormone (TSH) and a normal thyroxine level is commonly associated with endocrine abnormalities in pregnancy. Anti-thyroperoxidase (anti-TPO) antibody having the ability to cross the placenta

ISSN: 0975-3583, 0976-2833 VOL08, ISSUE 02, 2017

has been suggested to affect fetal growth. Euthyroid pregnant women with high anti-TPO antibody titers have been registered with several adversities in obstetric and fetal outcomes. For women known to have hypothyroidism, an increase in thyroxine dose by 20–40% when pregnancy is confirmed usually ensures they remain euthyroid. Treatment of subclinical hypothyroidism is recommended if the woman has antithyroid antibodies [1-6]. Thyroid function tests are checked every month and every two weeks following a change in dose. Women with thyroid disorders in pregnancy should be followed up by their GP in the postpartum period. Postpartum thyroiditis may present months after delivery. Hence we have taken up this study to evaluate thyroid disorders in pregnancy. The aim and objective of the study is to determine the prevalence of thyroid disorders in pregnancy.

MATERIALS AND METHODS: This cross-sectional study was conducted in the Department of Obstetrics and Gynecology, Gouri Devi Institute of Medical Sciences & Hospital, Durgapur, WB

Study design: Prospective hospital based study.

Sample size: 800 cases of antenatal mothers were included.
Inclusion Criteria: Apparently healthy pregnant women, both primigravida and multi-gravida, with singleton pregnancies were included and written informed consent were obtained from the enrolled cases.
Exclusion Criteria: Pregnant women with preexisting thyroid diseases or any other endocrine disorders, pre-existing diabetes, on any hormone replacement therapy, any other metabolic or chronic disorders, and bad obstetric history with a known cause were excluded from the study.

Data collection: Detailed history was taken regarding the symptoms of thyroid disorders, menstrual history, obstetric history, past medical history, family history, personal and social history. General examination was done. Body temperature, pulse rate, blood pressure, respiratory rate was noted. Systemic examination of the cardiovascular system (CVS), central nervous system (CNS), respiratory system and thyroid gland was done.

Blood Sample Collection and Biochemical Investigations: Basic hematological and biochemical investigations were carried out along with thyroid function tests (TSH, FT3, FT4, anti TPO antibody titers). All the patients were subjected to first trimester ultrasound scan to confirm gestational age less than 12 weeks. The reference interval for thyroid panel were as per ATA guidelines. Thyroid profiles were done by the chemiluminescence method. For this study, the trimester-specific upper limit value for TSH was taken as <2.5 mIU/mL for the first trimester and <3 mIU/mL for the second and third trimesters as per American Thyroid Association (ATA) 2011 criteria. Patients with TSH levels higher than the trimester specific level and normal fT4 levels were diagnosed with SCH. Anti-TPO level <60 U/L was taken as normal upper limit as per manufacturer's protocol. Level more than 60U/L is considered a raised anti-TPO titer.

This cross-sectional study was conducted in the Department of Biochemistry, in collaboration with the Department of Obstetrics and Gynecology, and 382 eligible pregnant women coming for their first antenatal checkup (ANC) were enrolled in the study.

Apparently healthy pregnant women, both primigravida and multi-gravida, with singleton pregnancies in their first ANC were included and written informed consent was obtained from the enrolled cases. Pregnant women with preexisting thyroid diseases or any other endocrine disorders, pre-existing diabetes, on any hormone replacement therapy, any other metabolic or chronic disorders, and bad obstetric history with a known cause were excluded from the study. After general and gynecological examination, fasting, one-hour, and two-hour blood samples were collected for 75 g OGTT and estimation of thyroid profile (TSH, fT4, anti-TPO antibody). The biochemical parameters were performed on the Beckman Coulter AU5A00 auto analyzer with commercially available kits. Thyroid profiles were done by the chemiluminescence method in an Siemens Advia Centaur automated Immunoassay analyzer.

For this study, the trimester-specific upper limit value for TSH was taken as <2.5 mIU/mL for the first trimester and <3 mIU/mL for the second and third trimesters as per American Thyroid Association (ATA) 2011 criteria. Patients with TSH levels higher than the trimester specific level and normal fT4 levels were diagnosed with SCH. Anti-TPO level <60 U/L was taken as normal upper limit as per manufacturer's protocol. Level more than 60U/L is considered a raised anti-TPO titer. GDM was diagnosed using 75 g of glucose challenge test (GCT) with a fasting value of more than 92 mg/dl, a one-hour post-glucose value of more than 180 mg/dl, and a two-hour post-glucose value of more than 153

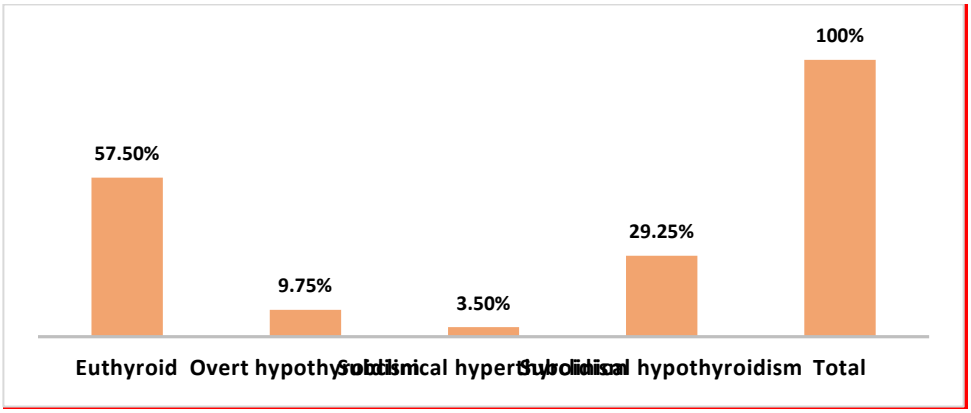
mg/d

RESULTS: This cross-sectional study was conducted in the Department of Obstetrics and Gynecology at our hospital. A total of 800 eligible pregnant women coming for their first antenatal checkup (ANC) were enrolled in the study.

Table 1: Shows baseline characteristics of the study patients

Parameters	Mean ± SD
Age	28.60 ± 3.89
Gestational age	8.98 ± 3.12
TSH	2.46 ± 1.78
FT3	2.3 ± 0.92
FT4	1.30 ± 0.67

Figure 1: Shows the frequency of various thyroid disorders in the study population



ISSN: 0975-3583, 0976-2833 VOL08, ISSUE 02, 2017

DISCUSSION:

In the present study, we enrolled a total of 800 antenatal mothers based on inclusion and exclusion criteria attending the OPD of OBG department at our tertiary care hospital. We measured thyroid function tests (TSH, FT3 and FT4 levels) to calculate and study the prevalence of subclinical hypothyroidism and overt hypothyroidism in pregnant women. We found the prevalence of 9.75% overt hypothyroidism, 9.75% overt hyperthyroidism, 3.5% subclinical hyperthyroidsim and 29.25% subclinical hypothyroidism. Further we evaluated for anti TPO antibodies, we found that the titres were elevated (>60 U/L) in 28% euthyroid pregnant women, 59% of overt hypothyroidism pregnant women and 73% of subclinical hypothyroidism pregnant women.

Primary maternal hypothyroidism is characterized by an increase in the serum TSH levels during pregnancy. It is further classified as subclinical hypothyroidism (SCH) which has normal free T4 levels and overt hypothyroidism (OH) which has decreased free T4 levels. This differentiation is crucial as it has clinical and management implications. Maternal complications reported to be associated with overt hypothyroidism include pre-eclampsia, placental abruption, polyhydramnios, oligohydramnios, hyperemesis, gestational diabetes, premature rupture of membranes, and chronic hypertension. For the fetus too, there is a high risk of fetal death, prematurity, low birth weight, congenital malformations, foetal distress, perinatal hypoxic encephalopathy, and deficit in the mental developmental coefficient. Some epidemiological studies have also pointed towards the association of maternal hypothyroidism and adverse neurological outcomes in the progeny ranging from neurological cretinism, congenital hypothyroidism, to decreased intelligence quotient.

The prevalence of SCH in pregnancy differs extensively worldwide. In India, the prevalence of SCH varies from 2.8% to 32.94% in different parts of the country, as documented in various studies. Gayathri et al. reported the prevalence of SCH of 2.8% among pregnant women in Chennai and 57.1% of the subclinical hypothyroid patients had positive TPO antibodies. Aggarwal et al. documented the prevalence of SCH to be 10.9% among pregnant women in a study conducted in a premier institute in north India, and TPO antibody positivity was 59% among the subclinical hypothyroid pregnant women in their study.

Hypothyroidism in pregnancy: For women with overt hypothyroidism who are planning for pregnancy, guidelines recommend optimisation of TSH before conception. Thyroid dysfunction in pregnancy is clinically important as insufficient thyroxine is associated with an increased risk of premature birth, low birth weight and miscarriage. After conception, an increase in thyroxine as soon as possible is recommended with the goal of normalising the TSH concentration. An easy approach is to increase the total weekly thyroxine dose by an extra two tablets per week or by 20–30% of the baseline dose when pregnancy is confirmed. Serum TSH should be monitored every four weeks in the first trimester to ensure the woman is euthyroid, and then six to eight weekly therafter. Thyroid function tests should be rechecked four weeks after any dosage adjustments to ensure euthyroid levels are maintained. Aim to maintain TSH in the range 0.5–2.5 mIU/L. Failure to achieve a euthyroid state despite appropriate therapy necessitates investigation into causes for a lack of thyroxine uptake. This can result from poor adherence to therapy or impaired absorption. Women should be advised to take their thyroxine on an empty stomach before breakfast. There should be a 4–5-hour

ISSN: 0975-3583, 0976-2833 VOL08, ISSUE 02, 2017

gap before taking medicines such as vitamins, calcium and iron tablets as interactions in the gastrointestinal tract can reduce thyroxine absorption. Following delivery, the thyroxine dose should be reduced to the patient's preconception dose, assuming the woman was euthyroid on that dose. Check thyroid function tests 4–6 weeks after their dose has been reduced postpartum [7-10].

Overt hypothyroidism in pregnancy: A new diagnosis of overt hypothyroidism should warrant immediate thyroxine replacement and further investigation for the presence of thyroid auto-antibodies: antithyroid peroxidase antibodies (antiTPO), antithyroglobulin antibodies (TgAb), thyrotropin receptor antibodies (TRAb) (if there is a history of treated Graves' disease). The usual starting dose of thyroxine is at least 50 micrograms per day with maintenance between 100 and 150 micrograms per day. The starting dose of thyroxine will depend on the degree of hypothyroidism, the size of the patient and the presence of other medical problems. If unsure, the most important thing is to check thyroid function soon after starting therapy (e.g. at 4 weeks) and up-titrate the dose aiming to achieve a TSH below 2.5 mIU/L as quickly as possible [11-13].

Subclinical hypothyroidism in pregnancy: Subclinical hypothyroidism in pregnancy is associated with an increased risk of recurrent miscarriage, intrauterine growth restriction, preterm birth, low birth weight, perinatal mortality and pre-eclampsia. Thyroxine may reduce associated risks. Recent studies support thyroxine replacement in women with subclinical hypothyroidism undergoing assisted reproduction technologies, to improve pregnancy outcome. The aim of treatment is to achieve a TSH less than 2.5 mIU/L. Women with subclinical hypothyroidism should be tested for antithyroid antibodies as this impacts on the effects in pregnancy and may also be associated with other autoimmune conditions such as type 1 diabetes. At present, there are no data to support treating pregnant women who have subclinical hypothyroidism if they do not have antibodies. Previous guidelines recommended giving thyroxine to all women with subclinical hypothyroidism, regardless of their antibody status. This was due to research which reported multiple maternal and neonatal adverse outcomes associated with subclinical hypothyroidism, however the role of thyroxine therapy in preventing these outcomes was unclear.

Hyperthyroidism in pregnancy: Medical therapy is recommended in women with overt hyperthyroidism due to Graves' disease, toxic adenoma or toxic multinodular goitre. For these women, the aims of therapy are to use the lowest dose of antithyroid drugs to minimise maternal and fetal adverse effects. The dose should be adjusted to keep maternal serum fT4 at the upper limit of the normal range to minimise the risk of fetal hypothyroidism. Both propylthiouracil and carbimazole cross the placenta and have implications in fetal development. The risks include fetal goitre and transient hypothyroidism. Both drugs can cause maternal agranulocytosis. Propylthiouracil is recommended as the first-line antithyroid drug in the first trimester as carbimazole is associated with congenital abnormalities [14-16].

CONCLUSION: Thyroid dysfunction during pregnancy and the postpartum period is a common obstetric problem primarily managed by GPs. At-risk women are screened, but universal thyroid function screening is currently not recommended during pregnancy or postpartum. Thyroxine is used for treating overt hypothyroidism and is recommended in

antibody positive subclinical hypothyroidism. For hyperthyroidism, propylthiouracil is the preferred antithyroid drug in the preconception and first trimester to reduce the risk of teratogenicity. Carbimazole may be used in the second trimester. This present study revealed an increase in subclinical hypothyroidism in pregnancy in our population. A significant number of SCH with high anti-TPO antibody titer points towards autoimmunity as being a significant cause of the decreased level of thyroid hormones in pregnancy.

We declare no financial support (self-funding) and nil conflict of interest.

REFERENCES:

1. Lazarus JH. Thyroid function in pregnancy. *Br Med Bull* 2011;97:137-48.
2. Abalovich M, Amino N, Barbour LA, Cobin RH, De Groot LJ, Glinoer D, et al. Management of thyroid dysfunction during pregnancy and postpartum: an Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab* 2007;92 Suppl:s1-47.
3. Fan X, Wu L. The impact of thyroid abnormalities during pregnancy on subsequent neuropsychological development of the offspring: a meta-analysis. *J Matern Fetal Neonatal Med* 2016;29:3971-6.
4. Patil-Sisodia K, Mestman JH. Graves hyperthyroidism and pregnancy: a clinical update. *Endocr Pract* 2010;16:118-29.
5. Krassas GE, Poppe K, Glinoer D. Thyroid function and human reproductive health. *Endocr Rev* 2010;31:702-55.
6. Alexander EK, Pearce EN, Brent GA, Brown RS, Chen H, Dosiou C, et al. 2017 Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and the postpartum. *Thyroid* 2017;27:315-89.
7. Women's Health Committee; The Royal Australian and New Zealand College of Obstetricians and Gynaecologists. Testing for hypothyroidism during pregnancy with serum TSH [Internet]. Melbourne: Royal Australian and New Zealand College of Obstetricians and Gynaecologists; 2015.
8. 8. Yassa L, Marqusee E, Fawcett R, Alexander EK. Thyroid hormone early adjustment in pregnancy (the THERAPY) trial. J Clin Endocrinol Metab 2010;95:3234-41.
9. National Health and Medical Research Council, Australian Government Department of Health and Ageing, New Zealand Ministry of Health. Nutrient reference values for Australia and New Zealand including recommended dietary intakes. Canberra: NHMRC; 2006.
10. Alexander EK, Marqusee E, Lawrence J, Jarolim P, Fischer GA, Larsen PR. Timing and magnitude of increases in levothyroxine requirements during pregnancy in women with hypothyroidism. N Engl J Med 2004;351:241-9. A
11. Lazarus J, Brown RS, Daumerie C. Hubalewska- Dydejczyk A, Negro R, Vaidya B. 2014 European thyroid association guidelines for the management of subclinical hypothyroidism in pregnancy and in children. Eur Thyroid J 2014;3:76-94.

ISSN: 0975-3583, 0976-2833 VOL08, ISSUE 02, 2017

12. 12. Stagnaro-Green A. Postpartum management of women begun on levothyroxine during pregnancy. Front Endocrinol (Lausanne) 2015;6:183
13. Devdhar M, Ousman YH, Burman KD. Hypothyroidism. Endocrinol Metab Clin North Am 2007;36:595-615.
14. Earl R, Crowther CA, Middleton P. Interventions for hyperthyroidism pre-pregnancy and during pregnancy. Cochrane Database Syst Rev 2013;CD008633
15. Taylor PN, Vaidya B. Side effects of anti-thyroid drugs and their impact on the choice of treatment for thyrotoxicosis in pregnancy. Eur Thyroid J 2012;1:176-85.
16. Glatstein MM, Garcia-Bournissen F, Giglio N, Finkelstein Y, Koren G. Pharmacologic treatment of hyperthyroidism during lactation. Can Fam Physician 2009;55:797-8.