Review Article

Obstetric controversies in thyroidology

Ambika Gopalakrishnan Unnikrishnan, Shilpa Bhosale, Sanjay Kalra[1]
Departments of Endocrinology and Diabetes, Chellaram Diabetes Institute, Pune, [1]Bharti Research Institute of Diabetes and Endocrinology, Karnal, Haryana, India

ABSTRACT

It is well known that thyroid disorders commonly affect women. The care of pregnant women affected by thyroid disease is an important clinical challenge for endocrinologists. Hypothyroidism is the commonest problem, and maternal hypothyroxinemia has been linked to adverse feto-maternal outcomes. This article would discuss the controversy regarding first-trimester thyroid hormone deficiency and fetal brain development. Certain obstetric controversies in the management of hyperthyroidism in pregnancy, including the indications of TSH receptor antibody measurements and fetal thyroid status monitoring would also be discussed.

Key words: Hypothyroidism, hyperthyroidism, pregnancy

Introduction

Thyroid disease, especially hypothyroidism, is very common in India, especially in women.[1-4] Hypothyroidism is commoner in women than men. Positivity to thyroid antibodies is also common in the general population, particularly in women. This article on obstetric controversies in thyroidology will focus on hypothyroidism and autoimmune disease. Being part of a mini-review series, this article will not provide an extensive review of the subject, but would rather cover selected controversies of interest to the practicing endocrinologist.

Understanding Risk in Maternal Hypothyroxinemia

In general, studies have suggested that early maternal hypothyroxinemia affects the offspring subject, as the fetal brain development occurs in the first trimester, and because fetal thyroid gland develops after the 12th week. This has often put clinicians in a quandary, as patients often present with pregnancy and very high TSH values, and gynecologists are often considering termination of pregnancy in view of hypothyroidism. As there are no Indian studies correlating maternal hypothyroxinemia and fetal risk, we must continue to rely on international data. From these, international research papers, it is well known that - (a) untreated hypothyroidism in pregnancy may lead to lowered intelligence quotient in the offspring (b) children born to mothers with untreated hypothyroidism had higher learning disabilities and (c) iodine deficiency in pregnancy can also lead to neuropsychological problems in offspring.[5,6] Iodine deficiency in Indian women has been variably reported as low or high.[7]

Access this article online	
Quick Response Code:	Website: www.ijem.in
	DOI: 10.4103/2230-8210.119498

Is Medical Termination Of Pregnancy (MTP) Justified In Maternal Hypothyroidism?

In order to understand this, it is important to analyze the MTP act of 1971.[8] According to this act, MTP can be advised up to 12 weeks, and the decision can be made by one qualified doctor. In case two qualified doctors can concur, MTP can be done up to 20 weeks. From the list of qualifications to be categorized as a doctor qualified to advise or perform MTP, it is clear that being an endocrinologist does not qualify a doctor as far as MTP is concerned. MTP is generally performed to save the life of the mother, for social indications and for what is termed "eugenic" reasons. Eugenic indications are

Corresponding Author: Dr. Ambika Gopalakrishnan Unnikrishnan, Department of Endocrinology and Diabetes, Chellaram Diabetes Institute, Pune, Maharashtra, India. E-mail: uag@cdi.org.in

when there is a substantial potential of a baby being born with serious mental or physical disability. These reasons include-anencephaly, chromosomal disorders Down's syndrome, genetic diseases like hemophilia and exposure to teratogens, radiation, and rubella. The term hypothyroidism is not listed.

Obviously, it is better to discuss the current state of evidence with the patient. However, some generalizations come to mind-if the pregnancy is more than 20 weeks, there is no doubt that MTP should not be done. Similarly, in cases of subclinical hypothyroidism too, there is no indication for MTP.[9] In 'severe' cases of hypothyroidism where the conception has occurred without difficulty-the benefits and risks may be discussed with the patient-and unless there is a request from the patient, MTP cannot be recommended for hypothyroidism. In the management of hypothyroidism in pregnancy it may be remembered that the baby's intelligence quotient is not the sole overriding consideration and that there are other problems that can be a consequence of hypothyroidism in pregnancy. This includes miscarriages, pre-eclampsia, anemia, abruptio placentae, and postpartum hemorrhage.[10,11]

Hyperthyroidism in Pregnancy and Areas of Controversy

This article will assume that readers are familiar with the following aspects of managing hyperthyroidism in pregnancy-the need to treat with the minimum dose of anti-thyroid drugs to keep the TSH normal and the FT4 in the upper half of the normal range, the need to monitor maternal and fetal health and the current guidelines that suggest the use of propylthiouracil in the first trimester and carbimazole/methimazole in the rest of pregnancy, as well as the trimester specific TSH cutoffs in pregnancy. One area of ambiguity is the need for a recommendation on TSH-receptor antibody testing in pregnancy. Recently, a review has suggested that international consensuses are concordant about the indications for TSH-receptor (TSHR) antibodies in pregnancy.[12-14] In a pregnant patient on anti-thyroid drugs, known to have Graves' disease, TSHR antibodies must be measured during the 22nd week. In pregnant women with a past history of Graves' disease treated with radio-iodine or surgery-TSHR must be measured at about 22-28 weeks. Finally, TSHR may also be measured in mothers with a previous history of TSHR antibody positivity, and also in mothers with previous history of neonates born with neonatal thyrotoxicosis. Is there a need for fetal monitoring in thyrotoxicosis, and if so, what are the fetal ultrasound criteria to be used? This has long been unclear and present guidelines have attempted to shed light on this clinically relevant issue. Fetal ultrasound should look for fetal heart rate and fetal goiter both signaling that the anti-thyroid drugs may have crossed the placenta and also for signals of hyperthyroidism like fetal tachycardia, intrauterine growth retardation, and features like advancing bone age as well as fetal hydrops. It is best that fetal ultrasounds be done when the TSHR antibodies are more than 2-3 folds higher than normal, and from the 18th to the 22nd week of gestation. After fetal surveillance is begun, the TSHR antibodies may need to be tested every 6 weeks or so. In the preceding lines, the article has looked at what happens if TSHR antibodies and anti-thyroid drugs cross placenta. A third possibility is that of thyroxine crossing the placenta: This happens in cases of severe, long-standing thyrotoxicosis. This may suppress the pituitary of the fetus and thus, after birth the suppressed pituitary may take a while to recover-resulting in a period of transient-central hypothyroidism. This suggests that babies of hyperthyroid mothers need to be screened with TSH and Free T4 estimations. A final issue in question has been the use of anti-thyroid drugs in lactation. This has been recently settled, with studies showing that neither methimazole 30 mg/day nor propylthouracil 300 mg per day has any detrimental effect on the breast-feeding neonate's thyroid function. However, the drug of choice is methimazole/carbimazole-so that the liver of the baby as well as the mother may be protected from liver necrosis attributable to propylthiouracil.

Future Directions

In general, the thyroid gland has not received the importance that it deserves-the diseases being so common and widespread.[15,16] Other than hyperthyroidism and hypothyroidism, other thyroid diseases also require study such as for instance thyroid nodules. Clinicians are also aware of the occurrence of thyroid nodules that enlarge in pregnancy; if the lesion is suspicious for malignancy, thyroidectomy may be considered in the 2nd trimester, but if diagnosed later then surgery may be done after delivery and suppressive thyroxin treatment instituted.[17,18] A third obstetric controversy is the hyperthyroidism and treatment during pregnancy as well as lactation. Further research is required to establish answers to some of the controversies in the management of thyroid disease in pregnancy.

References

1. Unnikrishnan AG, Kalra S, Sahay RK, Bantwal G, John M, Tewari N. Prevalence of hypothyroidism in adults: An epidemiological study in

eight cities of India. Indian J Endocr Metab 2013;17:647-52.
2. Unnikrishnan AG, Menon UV. Thyroid disorders in India: An epidemiological perspective. Indian J Endocrinol Metab 2011;15:S78-81.
3. Usha Menon V, Sundaram KR, Unnikrishnan AG, Jayakumar RV, Nair V, Kumar H. High prevalence of undetected thyroid disorders in an iodine sufficient adult south Indian population. J Indian Med Assoc 2009;107:72-7.
4. Menon VU, Chellan G, Sundaram KR, Murthy S, Kumar H, Unnikrishnan AG, *et al*. Iodine status and its correlations with age, blood pressure, and thyroid volume in South Indian women above 35 years of age (Amrita Thyroid Survey). Indian J Endocrinol Metab 2011;15:309-15.
5. Haddow JE, Palomaki GE, Allan WC, Williams JR, Knight GJ, Gagnon J, *et al*. Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. N Engl J Med 1999;341:549-55.
6. Pop VJ, Brouwers EP, Vader HL, Vulsma T, van Baar AL, de Vijlder JJ. Maternal hypothyroxinemia during early pregnancy and subsequent child. Clin Endocrinol (Oxf) 2003;59:282-8.
7. Ahad F, Ganie SA. Iodine, iodine metabolism and Iodine deficiency disorders revisited. Indian J Endocrinol Metab 2010;14:13-7.
8. The Medical Termination of Pregnancy Act, 1971 (Act No. 34 of 1971). Available from: http://bhind.nic.in/Sparsh_MTP-Act-1971.pdf [Last accessed on 2012 Sep 1].
9. Kalra S, Ganie MA, Unnikrishnan AG. Overt hypothyroidism in pregnancy: Can we consider medical termination of pregnancy? Indian J Endocrinol Metab 2013;17:197-9.
10. Nambiar V, Jagtap VS, Sarathi V, Lila AR, Kamalanathan S, Bandgar TR, *et al*. Prevalence and impact of thyroid disorders on maternal outcome in Asian-Indian pregnant women. J Thyroid Res 2011;2011:429097.
11. Sahu MT, Das V, Mittal S, Agarwal A, Sahu M. Over and subclinical thyroid dysfunction among Indian pregnant women and its effect on maternal and fetal outcome. Arch Gynecol Obstet 2010;281:215-20.
12. Alamdari S, Azizi F, Delshad H, Sarvghadi F, Amouzegar A, Mehran L. Management of hyperthyroidism in pregnancy: Comparison of recommendations of american thyroid association and endocrine society. J Thyroid Res 2013;2013:878467.
13. Stagnaro-Green A, Abalovich M, Alexander E, Azizi F, Mestman J, Negro R, *et al*. American Thyroid Association Taskforce on Thyroid Disease During Pregnancy and Postpartum. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. Thyroid 2011;21:1081-125.
14. De Groot L, Abalovich M, Alexander EK, Amino N, Barbour L, Cobin RH, *et al*. Management of thyroid dysfunction during pregnancy and postpartum: An endocrine society clinical practice guideline. J Clin Endocrinol Metab 2012;97:2543-65.
15. Kalra S, Unnikrishnan AG, Sahay R. Thyroidology and public health: The challenges ahead. Indian J Endocrinol Metab 2011;15:S73-5.
16. Kalra S, Unnikrishnan AG, Baruah MP. Thyroid: Disorders of a lesser gland. Thyroid Res Pract 2013;10:45-6.
17. Unnikrishnan AG, Kalra S, Baruah M, Nair G, Nair V, Bantwal G, *et al*. Endocrine Society of India management guidelines for patients with thyroid nodules: A position statement. Indian J Endocrinol Metab 2011;15:2-8.
18. Tan GH, Gharib H, Goellner JR, van Heerden JA, Bahn RS. Management of thyroid nodules in pregnancy. Arch Intern Med 1996;156:2317-20.

Cite this article as: Unnikrishnan AG, Bhosale S, Kalra S. Obstetric controversies in thyroidology. Indian J Endocr Metab 2013;17:S29-31.

Source of Support: Nil, **Conflict of Interest:** None declared.