Editorial

Ensuring an intelligent India: Managing hypothyroidism in pregnancy

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Hypothyroidism is a disorder commonly encountered in pregnancy. While thyroid antibodies are present in up to 15% of women in the reproductive age group, overt hypothyroidism is noted in 0.3-0.5% of all pregnancies, and subclinical hypothyroidism in 2-3%.[1] The pregnant woman presents a unique challenge, as well as an unparalleled opportunity, for the thyroidologist.

Hypothyroidism may be difficult to diagnose in pregnancy, as most of the clinical features are nonspecific (asthenia, lethargy), or may be masked by obstetric symptoms (increase in weight, altered appetite). The various clinical scoring systems discussed in this issue are valid only for non-pregnant adults, and cannot be used in the antenatal outpatient department.[2]

Because of the nonspecific nature of its symptoms, hypothyroidism needs to be diagnosed by thyroid function tests. While some authorities recommend targeted case-finding,[3] others point out that 30% of all hypothyroid women will be missed by this approach. Others suggest universal screening for hypothyroidism in pregnancy, and are able to detect 1 hypothyroid patient in every 40 antenatal mothers screened.[4]

Screening in pregnancy is done using serum TSH. An elevated TSH indicates primary hypothyroidism, and serum-free T4 levels will help to categorize this as either overt or subclinical hypothyroidism. Thyroid antibodies may be measured to confirm Hashimoto's thyroiditis, which is the most common cause of hypothyroidism in pregnancy.[3]

All this, however, is easier said than done. Reference ranges for thyroid hormones are different in non-pregnant and pregnant individuals. Normal values of these hormones also vary from trimester to trimester. Total T3 and T4 are raised in pregnancy, due to a two fold increase in thyroxine binding globulin. The normal total T4 range, therefore should be multiplied 1.5 times, to obtain appropriate ranges for the second and third trimesters. Free T4 estimation is preferred in pregnancy, but this too, is influenced by changes in serum albumin and TBG, and is not without limitations. No consensus has been reached on trimester-specific or laboratory specific normal values of serum free T4 in pregnancy yet.[5] The Endocrine Society (USA) guidelines recommend "caution in the interpretation of serum free T4 levels during pregnancy."[3]

Similar caution is also required while interpreting TSH values. Several factors, including a negative feedback because of elevated T3 and T4, elevated circulating human chorionic gonadotropin concentrations influence the TSH levels.

The normal values of TSH are lower in pregnancy than in non-pregnant adults, and may be suppressed to the so-called thyrotoxic levels in normal pregnant women, especially in the first trimester.[6] Differentiating gestational thyrotoxicosis from Graves' disease is necessary in order to prevent mismanagement of such patients.[6]

In view of these, awareness has to be created, among obstetricians, physicians, and endocrinologists, about the "normal" TSH, and target TSH values in pregnancy.

While hypothyroid women experience decreased fertility, those who do conceive run a higher risk of various

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obstetric illness. These include abortion, pregnancy–induced hypertension, placental abruption, and post-partum hemorrhage. Their unborn fetuses are also exposed to adverse outcomes due to premature birth and low birth weight.[6] There is ample understanding among the obstetrician fraternity about these issues, as well as the need to treat hypothyroidism to prevent these complications.

What is not so well understood, however, is the effect of hypothyroidism on the fetal brain development and on the future psychoneurological status of the unborn children.

Thyroid hormones contribute immensely to the development of the fetal brain. While the fetal thyroid begins to function at 12 weeks gestational age, maternal thyroxine is present in the fetal brain as early as 8 weeks gestation.[7] Thus, it stands to reason that maternal hypothyroidism will negatively impact the initial development of the fetal brain.

This was observed four decades ago by Evelyn Man *et al*, who reported reduced intelligence quotients (IQ) in children born to hypothyroid mothers. A large prospective study published in 1999 reported that such children had an IQ 7 points below mean IQ of children of euthyroid women.[8] Progeny of hypothyroid women were three times as likely to have learning disabilities than children of euthyroid mothers.[9] Similar results have been reported from USA and the Netherlands.[10,11]

Even greater disability has been reported in children of women residing in iodine-deficient areas. Such reports come from Spain, various regions of Italy, Iran, as well as India.[12] In this clinical situation, both maternal and fetal hypothyroidism are present, while in maternal Hashimoto's thyroiditis, fetal thyroid function is normal.

Kalra, Sahay and Unnikrishnan, reviewing public health and thyroidology in this issue of IJEM, focus on the need for optimal management of hypothyroidism in pregnancy.[13] This is one area of thyroidology which can never be over emphasized.

Universal screening for hypothyroidism in early pregnancy should be advocated. Awareness should be spread among all stakeholders, including obstetricians, endocrinologists, physicians, and laboratory medicine personnel, about the different pregnancy-specific and trimester-specific ranges for thyroid hormones.

A TSH of 2.5 mIU/ml or less should be targeted, from the first antenatal visit onward, in all patients.

A concerted effort on part of all involved medical personnel, will lead to an improvement in maternal and neonatal health. More importantly, it will help improve the IQ of the unborn generations of India, and the whole world. Ensuring adequate iodine intake, and prescribing a simple tablet of thyroxine, when indicated, has the potential to ensure an intelligent India, and an intelligent world, in future.

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