Editorial

Overt hypothyroidism in pregnancy: Can we consider medical termination of pregnancy?

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Thyroidology has made rapid strides in recent times. The rapidity of advances has also brought with it certain controversies regarding the optimal management of thyroid disorders in pregnancy. Detailed guidelines for managing thyroid dysfunction during pregnancy are available from India as well as abroad.[1-3] These documents describe the management of various thyroid disorders, including maternal hypothyroidism and its impact on maternal, fetal, and long-term neuropsychological effects.

Most guidelines, however, are silent on one vexing aspect of management: Whether or not to, and when to advise medical termination of pregnancy (MTP) to an antenatal mother presenting in early pregnancy with overt hypothyroidism (OH). The Indian Thyroid Society guidelines do mention that maternal hypothyroidism is in itself not an indication for MTP. However, the guidelines do not expand upon this fairly common clinical dilemma.

Hypothyroidism in Pregnancy

The epidemiology of hypothyroidism has been discussed earlier in IJEM by Unnikrishnan, *et al*.[4] Hypothyroidism is especially frequent in going women of child-bearing age. Hence, it follows that hypothyroidism will be a frequent co-morbid condition in pregnancy.

While thyroid autoantibody positivity is seen in a large percentage of women of child-bearing age, the prevalence of subclinical hypothyroidism (SCH) and OH is lower. The commonest cause of hypothyroidism is Hashimoto's thyroiditis. Other causes include iodine deficiency, treatment with radioactive iodine ablation or by surgery, and lymphocytic hypophysitis.

A report from Chennai revealed a prevalence of 2.8% of SCH among 495 women without known thyroid disease. In the same study, 5 out of 500 screened women had a history of already diagnosed thyroid disease. The thyroid peroxidase antibody positivity was 57.1% in antenatal women with SCH and 7% in euthyroid antenatal women.[5] A similar report from Mumbai, studying 483 consecutive pregnant women in their first trimester, who were followed till delivery, found a 4.8% prevalence of hypothyroidism and 6.4% thyroid antibody positivity.[6] Researchers in Delhi, following up 633 women from second trimester onward, found a higher prevalence of 4.58%of OH, along with high risk of fetal and maternal complications.[7]

The Endocrinologist's Dilemma

Clinical symptoms of hypothyroidism are non-specific, and may be confused with routine obstetric complaints. Yet, other patients may be asymptomatic. The diagnosis of hypothyroidism in pregnancy, therefore, depends on biochemical thyroid function tests.

As some centers screen for hypothyroidism in high-risk patients and other centers opt for universal screening, the chances of encountering patients with "severe" OH, who are diagnosed during first or second trimester of pregnancy, are significant.

It is not uncommon for an endocrinologist to receive a referral from an obstetrician, requesting opinion for management of an antenatal patient with double digit thyroid stimulating hormone (TSH) values. Should the endocrinologist, knowing the potential adverse

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neuropsychological impact on the unborn offspring, advise medical termination of pregnancy? Or should the patient be put on high dose of thyroxine replacement, with a prayer for optimal fetal and long-term neuropsychological outcomes in the child? All guidelines are silent on this difficult, yet important, aspect of management of hypothyroidism in pregnancy. In the absence of randomized clinical trials or consensus guidelines to answer this challenging question, the endocrinologist is left to find an appropriate response by extrapolating data from available published literature. This editorial aims to deliberate upon this contentious issue.

Thyroid and Fetal Brain Development

That the thyroid hormone is necessary for fetal brain development and that the early fetus is dependent on maternal sources for its supply are beyond doubt.[8,9] Untreated or inadequately treated hypothyroidism in mothers has been shown to lead to birth of children with significantly lower intelligence quotients (1Q).[10,11] The incidence of learning disabilities is much higher in children born to women with untreated OH. Newer studies show that this dysfunction may be limited to specific components of intelligence. Different studies, however, pinpoint varying targets of maternal hypothyroidism: psychomotor development, verbal 1Q, and learning capacity. The impact of maternal hypothyroidism also depends on the level of iodine nutrition in a given patient. Recent results from Japan, which suggest no effect of suboptimal control of hypothyroidism in pregnancy on the neuropsychological development of offspring,[12] may not be relevant to iodine-deficient countries. While data from Kochi suggest that iodine levels are adequate in most Indian women, the same optimism is not shared by researchers from other parts of the country.[13,14]

While we do try to achieve the best possible outcome for all patients, the occurrence of OH, especially of a "great severity," in low-moderate iodine intake areas, poses an ethical dilemma. Knowing the possible consequences of OH on the fetus, and not fully knowing the potential consequences on the unborn offspring, should we allow patients who have conceived, without prior planning, while being overtly hypothyroid, to continue pregnancy till term? Or should we, if possible, seek an early termination of pregnancy, and plan conception after the patient is made euthyroid?

The Medical Termination of Pregnancy Act

In India, termination of pregnancy is advised according to the Medical Termination of Pregnancy Act, 1971. Let us see if the MTP Act provides any guidance for this particular field of obstetric endocrinology. The MTP Act allows for termination of pregnancy until 12 weeks of pregnancy, provided certain specific criteria are met, and the decision is taken by one qualified medical practitioner. It also allows MTP up to 20 weeks of gestation, if advised by two qualified doctors. The list of qualifications required to be eligible to advise or perform MTP does not include a degree in endocrinology.

MTP is indicated to save the life of the mother, for social indications, and for eugenic reasons. Eugenic indications are cited of there is a "substantial risk of the child being born with serious physical and mental abnormalities so as to be handicapped in life." This heading includes conditions such as structural abnormalities (anencephaly), chromosomal disorders (Down's), genetic diseases (hemophilia), exposure to teratogenic drugs, radiation, and rubella. There is no mention of OH in the list of indication for MTP.[15]

However, the definition of "serious mental abnormalities so as to be handicapped in life" is a qualitative one. In the present era of patient-centered care, the mother's opinion about possible psychoneurological impact on unborn offspring should be taken into account.

To take an example from obstetrics, the option of MTP is offered to patients with uncontrolled diabetes presenting with an unplanned conception, but there is no definitive HbA1c cut-off at which to make MTP mandatory. The choice is usually made by a process of shared decision making, keeping the patient's individual characteristics in mind. In later pregnancy, the triple marker test can be applied to assess the risk of Down's syndrome, trisomy 18, and neural tube defects. However, there is no definite value at which to enforce an MTP: the results can at best be considered suggestive of the fetal risk. Similarly, in pregnancy complicated by OH, the decision to continue or terminate pregnancy will vary from case to case based on multiple factors [Table 1].

Table 1: Factors influencing decisions for medical termination of pregnancy in hypothyroidism complicated pregnancy

Severity of hypothyroidism
Gestation gravity
Iodine nutrition status
Past h/o infertility
Past h/o miscarriage/fetal loss
Past h/o congenital malformation
Past h/o offspring with intellectual impairment
Patient's attitudes and beliefs regarding MTP
Family h/o congenital malformation
Family h/o intellectual impairment

MTP: Medical termination of pregnancy

Summary

Keeping the above discussion in mind, we suggest the following algorithm of management:

- Patients with SCH, at any gestation: Treat as per guidelines, with l-thyroxine. Do not consider MTP.
- Patients with OH, beyond 20 weeks gestation: Treat as per guidelines, with l-thyroxine. Do not consider MTP.
- Patient with OH, below 20 weeks gestation: Treat as per guidelines, with l-thyroxine. If conception has occurred without difficulty, and OH is "severe," take a final decision after discussing all aspects with the patient. MTP cannot be recommended at present unless there is a request from the patient.

Conclusion

Maternal hypothyroidism is relatively common and may not be diagnosed (and therefore not treated) during pregnancy. This may even remain undiagnosed for several months after delivery. Currently it seems unclear as to how detrimental this may be for the development of the neonate. The consequences of maternal hypothyroidism on the fetus or neonate are probably the result of interplay of several factors acting, such as decreased availability of maternal thyroid hormones at crucial times in fetal brain development, obstetric events associated with maternal hypothyroidism, and possibly prolonged concealed maternal hypothyroidism during pregnancy. Ethically important but debatable issue is whether clinicians should recommend terminating pregnancy when severe hypothyroidism is diagnosed late in gestation. Present consensus among obstetric care providers and endocrinologists is against recommending abortion, but despite the administration of thyroxine, future parents cannot be fully reassured about potential brain damage as a result of longstanding and severe intrauterine undiagnosed hypothyroidism. Keeping in view the nature of the condition, it seems highly unlikely that any randomized clinical trial will ever be done to assess the TSH level cut-off at which MTP must be the advised. Any discussion regarding this will necessarily court controversy, skirting with the gray zones of eugenics, ethics, public health, obstetrics, and endocrinology. Decision making will vary from region to region, depending on the level of iodine intake, and the frequency and severity of OH in pregnancy. It will also vary between clinicians, based on personal clinical experience, and from patient to patient, based on personal attitudes, beliefs, and practices regarding abortion. Often, the decision may be taken because of "non-endocrine" issues or other obstetric-related factors, with OH being just a contributory factor favoring MTP.

This editorial should stimulate constructive debate and meaningful research in this area so that an evidence-based consensus is evolved over a period of time.

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