Brief Communication

Subclinical hypothyroidism in the first trimester of pregnancy in North India

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ABSTRACT

Subclinical hypothyroidism based on population and trimester specific cut-offs is reported to complicate 1-2% of all pregnancies. Using the recent Endocrine Society guidelines of 2.5 mIU/L of Thyroid Stimulating Hormone as the upper level of normal in the first trimester the reported prevalence of subclinical hypothyroidism is much higher. Recent publications have also emphasized that there is considerable racial variation in the prevalence of thyroid disorders in pregnancy. Among published literature North Indian women appear to have the highest rates of subclinical hypothyroidism in the first trimester of pregnancy. More widespread use of universal screening and trimester specific ranges in pregnancy for thyroid hormonal assays will lead to a large number of North Indian women requiring treatment for thyroid disorders in pregnancy.

Key words: First trimester, North India, pregnancy, subclinical hypothyroidism

Subclinical hypothyroidism (SCH) is reported to have a prevalence of 1-2% of all pregnancies.[1] However, these older estimates of prevalence have been based on region, assay, and trimester-specific TSH cut-offs for the diagnosis of SCH. Recent Endocrine Society guidelines suggested 0.1 to 2.5 mIU/L as the 'normal' range for TSH values in first trimester.[1] Using the above cut-off for the diagnosis, there have been several studies showing a much larger prevalence of SCH and marked variation between different ethnic groups. The prevalence of any degree of hypothyroidism in pregnancy has varied from 12.3% (Finnish), 15.5% (American) to 35.3% (South American) in these recent studies.[2-4] In the American study with samples from over half a million pregnant women, there were significant differences in the prevalence of hypothyroid disorders among Asian American women (19.3%) compared to African Americans (6.7%) and Caucasians (16.4%).[3] This was similar to the findings of a small study (unpublished) conducted by us, in which we measured thyroid function tests in the first trimester among 200 pregnant women and found that 16.5% of women had TSH levels > 4 mIU/L and 53.5% had TSH levels ≥ 2 mIU/L.[5] Another small study from Delhi involving 172 normal pregnant women in first trimester (thyroid normalcy suggested by negative thyroid antibodies, clinical assessment, iodine sufficiency, and normal thyroid ultrasound) revealed that the first trimester range of TSH in Indian women to be between 0.6-5.0 mIU/L.[6]

That is why I read with interest the study by Dhanwal and colleagues from Delhi published in the March issue of the journal.[7] Using a TSH cut-off of 4.5 mIU/L, they demonstrated a prevalence of hypothyroidism of 14.3% in the first trimester of pregnancy. The mean first trimester TSH value among the 1000 pregnant women was 3.68 mIU/L and was similar to the previously mentioned study by Marwaha and colleagues from Delhi.[6] In the study by Dhanwal *et al.,* using the Endocrine Society first trimester cut-off for the diagnosis of SCH (>2.5 mIU/L) would have led to over 50% of pregnant women in Delhi being diagnosed with SCH. The Society guidelines suggest that all those diagnosed with SCH in pregnancy should be offered treatment regardless thyroid antibody status,

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despite no current evidence of benefits because the risks would be negligible.[1]

Preliminary data from the unpublished TULIP study (Thyroid dysfunction in Urban Ludhiana Pregnancies) presented last year at the Endocrine Society Annual meeting also suggests that the prevalence of thyroid dysfunction in North India is very high. The impact on obstetrical and neonatal outcomes in these pregnancies when untreated for SCH is similar to studies from other parts of the world.[8]

Considering these findings, I can make the following observations.

1. SCH in the first trimester of pregnancy (diagnosed using the Endocrine Society range for TSH) would have a prevalence of over 50% among pregnant women in North India (Delhi and Punjab) if universal screening in pregnancy was the norm. The recent Indian Thyroid Society guidelines have suggested that universal screening should be the norm[9]
2. The adverse pregnancy and neonatal outcomes among women who have TSH values of > 2.5 mIU/L in the first trimester is similar among North Indian women as in other populations studied despite its 15-fold higher prevalence[8]
3. In the absence of any data as of yet that treating antibody-negative SCH in pregnancy leads to lesser adverse outcomes, treatment choices would be individual. However, the benefits of offering treatment are likely to outweigh the benefits. The Indian guidelines are unclear about treating women with TSH between 2.5 to the upper normal non-pregnant limits
4. Once hard outcome data become available that treatment of SCH in pregnancy leads to better outcomes (one large NIH funded clinical trial ongoing,[10] likely results in 2016) and universal screening of pregnant women becomes the standard, there is likely to be tsunami of pregnant women requiring levothyroxine treatment
5. Another interesting aspect of the whole issue is the question if women in Delhi were being exposed to much higher intakes of dietary iodine compared to women elsewhere (like Kashmir) and this, in turn, was responsible for the high prevalence of SCH in pregnancy. Two papers also published in the same issue of the journal suggest this possibility. The paper by Grewal *et al.*, from the All India Institute in Delhi demonstrates that 72% of pregnant women in the first trimester have more than the required intake of dietary iodine.[11] This is in contrast to the paper by Charoo *et al.* from Kashmir, in which most pregnant women had normal dietary iodine intake.[12]

In conclusion, preliminary data from studies including the two studies published in the March issue of the journal have highlighted that North Indian women have a high prevalence of thyroid dysfunction in the first trimester of pregnancy. Impact of thyroid dysfunction on pregnancy outcomes appear to manifest with a TSH threshold of > 2.5 mIU/L in the first trimester rather than with a TSH range based on percentiles cut-off derived from apparently 'normal' pregnant women. The large burden of SCH in pregnancy may prove to be a major public health burden in North India once it becomes clear that adverse outcomes can be corrected with screening and early replacement of levothyroxine.

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