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Research Article

High prevalence of subclinical hypothyroidism in pregnant women in South India

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ABSTRACT

Background: Thyroid dysfunction is one of the commonest endocrinopathies seen in pregnancy and affects both maternal and fetal outcomes. There is little data available on its prevalence in Indian pregnant women. This study was conducted at Bhaskar medical college and hospital situated in a rural/suburban area near Hyderabad, Telengana, India. The aim of the study was to find out the prevalence of thyroid disease among pregnant women.
Methods: All consecutive pregnant women registered from January 2014 to December 2014 were included in the study. Morning samples of serum were tested for T_3, T_4 and TSH.
Results: A total of 1340 women were included in the study. 260 pregnant women (19.41%) had TSH values more than 3.0 mIU/L, the cut-off value used for upper limit of normal in this study. Out of these, 216 had normal T_4 value, hence labeled as subclinical hypothyroidism and 44 had low T_4, hence termed overt hypothyroidism. Three pregnant women had overt hyperthyroidism and 11 had subclinical hyperthyroidism. Nine women had low T_4 values-Isolated hypothyroidism.
Conclusions: Prevalence of thyroid disease in pregnancy was found to be higher in our patients, more so the sub clinical hypothyroidism.

Keywords: Pregnancy, Thyroid dysfunction, Overt and subclinical hypothyroidism & hyperthyroidism, Isolated hypothyroidism

INTRODUCTION

Normal thyroid function in pregnancy is needed for a normal maternal and fetal outcome. Pregnancy is associated with profound changes in thyroid function. HCG values are high in early trimester, α component of which has similarity to TSH, causing partial TSH suppression.[1] Hence the cut-off value taken for upper limit of normal is 2.5 m IU/L in 1st trimester as compared to later 2 trimesters when a higher cut off of 3.0 m IU/L is taken as normal. The thyroid gland itself enlarges by 10% in pregnancy in iodine-sufficient areas and more so in iodine insufficient areas.[2] Iodine requirement in pregnancy is increased from 150 mg/day to 200 mg/day due to increased renal loss caused by increased renal blood flow and increased GFR.

In pregnancy, thyroid function is modified in various ways - the reasons being increased TBG (due to increased estrogen and decreased plasma clearance), altered metabolism of natural thyroid hormones, increased loss of I_2 by kidneys (increased RBF & increased GFR), altered I_2 transfer from placenta.[3]

Thyroid hormone is critical for normal fetal brain development, neuronal multiplication, migration and structural organization, thus on future intellectual development.[4] Fetal thyroid gland starts producing hormones from 8-10 weeks of gestation and significant amounts after mid-gestation. The maternal thyroid hormones transferred through placenta are the main source for fetal growth and development.

Deficiency of thyroid hormone is associated with complications of spontaneous/threatened miscarriage, preeclampsia, gestational hypertension, preterm delivery, LBW, IUGR, oligohydramnios, placental abruption, high perinatal mortality. Neonatal hyperbilirubinemia, hypo- / hyper-thyroidism, congenital cretinism, neuropsychological and cognitive impairment have been reported too.[5] These children later may develop attention deficit and hyperactivity syndrome.[6]

The physiological changes of pregnancy mimic thyroid disease significantly - fatigue, sluggishness, constipation, edema may simulate hypothyroidism; heat intolerance, wide pulse pressure, tachycardia may mimic hyperthyroidism.[7]

Western literature shows a prevalence of hypothyroidism in pregnancy of 2.5% and hyperthyroidism in pregnancy prevalence of 0.1 to 0.4%.[5] There is paucity of data on prevalence of thyroid disorders in pregnancy in Indian women. A few reports show a prevalence of 4.8% to 11% amongst Indian pregnant population.[8-11] An effort was made to find out the prevalence of the various thyroid dysfunctions in pregnancy in our women in this study.

METHODS

This observational study was done at Bhaskar medical college and hospital, catering mainly to rural and suburban population near Hyderabad. This was done as a collaboration between the departments of obstetrics & gynecology and biochemistry after institutional ethical committee clearance.

Inclusion criteria - all pregnant women registered at our hospital between January to December 2014 were included in the study.

All subjects were subjected to the usual history taking, clinical examination and ante-natal profile of investigations, also thyroid function tests comprising serum total T_3 (Trithyrodothyroxine), total T_4 (Thyroxine) & TSH (Thyroid stimulating hormone) were done - samples were collected at the same time as other investigations between 8 AM to 11 AM.

The tests were done by the following methods:

Total T_3 & T_4 - Competitive chemi-luminescent immunoassay

TSH - Ultra sensitive sandwich chemi-luminescent immunoassay

The reference ranges of the test values used in this study were as per the 2011 guidelines of American Thyroid Association (ATA) for the Diagnosis and management of thyroid disease during pregnancy and postpartum.[4] As per Regulation 14.2 of ATA Guidelines, if trimester-specific ranges for TSH are not available in the laboratory, the following upper normal reference ranges are recommended: 1st trimester - 0.1 to 2.5 mIU/L, 2nd trimester - 0.2 to 3.0 mIU/L & 3rd trimester - 0.3 to 3.0 mIU/L.

In pregnancy, serum total T_4 measurement is recommended over direct immunoassay of free T_4. Because of alterations in serum proteins in pregnancy (raised TBG, TBA, and prealbumin) Free T_4 assay may yield lower values based on reference ranges established with normal non-pregnant sera.[12]

Also method-specific and trimester-specific reference ranges for direct immunoassays of FreeT4 have not been generally established. By contrast, Total T4 increase during the 1st trimester and the reference range throughout pregnancy is 1.5 fold that of the non-pregnant range.[13]

This has also been corroborated in the executive summary for management of thyroid dysfunction during pregnancy and postpartum by endocrine society clinical practice guidelines, 2012 in recommendation 1.1 which advises that the non-pregnant Total T4 range (5-12 mcg/ dl or 50-150 nmol/L) can be adapted in the 2nd and 3rd trimesters by multiplying this range by one and half-fold.[14]

RESULTS

The patients were divided into the following groups according to the thyroid function test results:[4,14]

		TSH (mIU/L)	T_4 (mcg/dl)	T_3
1)	Euthyroid	0.2-3.0	N	N
2)	Subclinical hypothyroidism	>3.0	N	N
3)	Overt hypothyroidism	>3.0	<7.5	
4)	Subclinical hyperthyroidism	<0.1	N	
5)	Overt hyperthyroidism	<0.1	>18	
6)	Isolated hypothyroidism	N	< 7.5	N

Table 1: Distribution of cases as per gravidity (n=1340).

Gravidity	No. of pregnant women	Percentage
G1	630	47
G2	482	36
G3 and above	228	17

Table 2: Distribution of cases according to age (n=1340).

Age group (years)	No. of pregnant women	Percentage
<20	455	34
20-25	576	43
26-30	269	20
>30	40	3

Table 3: Thyroid dysfunction in the pregnant women (n=1340).

Parameter	No. of cases	Percentage
I - Euthyroid	1056	78.73
II - Hypothyroidism (total)	261	19.41
Overt	44	3.28
Subclinical	217	16.13
III - Hyperthyroidism (total)	14	1.04
Overt	3	-
Subclinical	11	-
IV - Isolated hypothyroidism	09	0.67

DISCUSSION

There has been a debate for a long time about the upper limit of normal TSH during pregnancy. Recent guidelines by American Thyroid Association (ATA) and the national association of clinical biochemists have reduced this to 2.5 mIU/L in 1st trimester and 3.0 mIU/L in 2nd/3rd trimesters. This was done because it was seen that in more than 95% of rigorously screened euthyroid volunteers, the normal range was from 0.4 to 2.5 mIU/L.[15] This of course increases the disease frequency of hypothyroidism in pregnancy upto 5 fold.

There is a wide variation in the prevalence of hypothyroidism in pregnancy - 2.5% in the West to 11% in India.[16] It is more in Asian countries as compared to the West.[17]

There are few published Indian studies on this topic. Sahu et al. have done thyroid function in second trimester and reported prevalence of thyroid disorders, especially overt and subclinical hypothyroidism to be 6.47%.[9] Dhanwal et al. from Delhi in 2013 reported a hypothyroidism prevalence of 14.3%, with a cut off of 4.5 mIU/L as upper limit of normal in a cohort of 1000 pregnant women.[10] In another study from Delhi, Nangia AS et al. in 2013 reported a prevalence rate of 12% amongst 400 pregnant women in 2nd trimester at a cut off of 3.0 mIU/L as per ATA guidelines.[11] Our study in contrast has shown a prevalence of 19.4% with 3 mIU/L as cut off value.

Various reasons have been proposed for increased prevalence of hypothyroidism in pregnancy. Increased iodine intake in diet,[18] presence of goitrogens in diet as reported from studies in India,[19] deficiency of micronutrients like selenium and iron[20] are some of the reasons ascribed to high Hypothyroidism prevalence in India. An inter-relation of this high prevalence of thyroid disorders with a high prevalence of the other major endocrinopathy - diabetes mellitus, has to be explored further.

High prevalence of endemic fluorosis in our area may be a factor in high hypothyroidism in our area. Historically since 1800s it has been seen that fluoride is associated with goiter and fluoride is used for treatment of hyperthyroidism. In 2006, the National Research Council in USA in its report stated that "fluoride exposure in humans is associated with increased TSH levels and goiter prevalence, and altered T_4, T_3 concentrations" and it recommended that the effects of fluoride on various endocrine functions like thyroid and parathyroid activity, impairment of glucose tolerance and possibly timing of sexual activity.[21]

We had 9 cases (0.67%) of isolated hypothyroxinemia. Literature shows a prevalence of 1.3-2.3% in iodine-sufficient areas to 15-30% in iodine-depleted populations. Akboba et al. in 2014 from Turkey reported 38% prevalence out of 196 pregnant women in a multicenter study.[22] Further studies needed to know its true prevalence as well as any detrimental effects on feto-maternal health.

Prevalence of hyperthyroidism, both overt and subclinical in various studies have been reported to be around 1%. In one study by Sangita Nangia et al. in 2013 in two hospitals together in Delhi, a prevalence of 1-2% was found amongst 400 pregnant women.[18] In our study, 14 out of 1340 pregnant women had hyperthyroidism (1%).

One strong point about our study is that it is one of the larger studies being reported from India. The limitation is we did not include tests to determine the cause of this high prevalence of subclinical hypothyroidism.

Our study concludes that there is a high prevalence of thyroid dysfunction in pregnancy in India, majority being subclinical hypothyroidism, and Universal screening for hypothyroidism is highly desirable in our country.

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