Original Research Article

Importance of Screening for Thyroid Functions in Early Pregnancy: Should It Be Made Mandatory

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Abstract

Background: There is ongoing controversy over Universal screening for thyroid function in pregnant women .**Objective**: To study the thyroid profile of 200 first trimester pregnant women and to evaluate whether Thyroid function screening to be made mandatory or not. **Methodology**: 200 first trimester pregnant women attending department of Obstetrics and Gynaecology at A N Magadh Medical College & Hospital(ANMMCH),Gaya, Bihar ,India were included in the study . They were sent for Thyroid function testing. Depending on the hormone values, cases were grouped into:Euthyroidism,Subclinical Hypothyroidism,Overt Hypothyroidism,Subclinical Hyperthyroidism and Overt Hyper-thyroidism. **Result:** In our study 71 (35.5%%) cases found to have subclinical hypothyroidism, 1(0.5%) case was found to have subclinical hyperthyroidism, 7 (3.5%) cases found to have overt hypothyroidism and 1 (0.5%) case was found to have overt hyperthyroidism. 96 cases out of 200 belong to primipara group (48%) and this group had the highest rate of history of spontaneous abortion 7.5% .There is statistically significant association between parity and thyroid disorders. **Conclusion:** High cases of thyroid disorders in Indian pregnant women makes it necessary to screen all the pregnant women in early pregnancy so that timely treatment can be given and fetal and maternal complications can be avoided.The high prevalence of thyroid disorders in Indian pregnant women makes it necessary to screen all the pregnant women in early pregnancy.

Keywords: Overt Hyperthyroidism, Overt Hypothyroidism, Screening, Subclinical Hyperthyroidism, Subclinical Hypothyroidism.

Introduction

The thyroid is a small endocrine gland located in front of the trachea. It utilizes iodine to produce thyroid hormones which are essential for normal growth,development,maturation and regulation of metab-olism. Thyroid disorders are common endocrine disorders seen during pregnancy,but may go unnoticed due to non specific symptoms. Thyroid disorders include subclinical hypothyroidism, subclinical hyperthyroidism, overt hypothyroidism and overt hyperthyroidism. The most prevalent thyroid disorder in pregnancy is subclinical hypothyroidism[1].Thyroid physiology changes signific-antly during pregnancy and inadequate adaptation to these changes result in thyroid dysfunctions. In first trimester, human chorionic gonadotropin (hCG) stimulates the thyroid gland because of its structural resemblance to TSH[2].This results in temporary low TSH value. Also, in early pregnancy, increased estrogen concentration, stimulates increased production of thyroid binding globulin (TBG). This causes a considerable increase in total T3 and T4 values, although the free hormone level remains unchanged. To maintain this constant value of free thyroid hormones , the production of thyroid hormones increases by 30-50 %[3,4].There is increased renal blood flow and increased glomerular filtration rate which causes increased iodide clearance from plasma and hence increased iodine loss[4].The net effect is increased burden on thyroid gland to meet the increased maternal and fetal requirement. Thyroid gland increases by 10 % in size during pregnancy, in iodine replete areas and 20-40% in iodine deficient areas.It is thus not surprising that thyroid dysfunction arise frequently in pregnancy. Also, thyroid function test results of healthy pregnant women differ from that of healthy non pregnant women. This calls for pregnancy specific and ideally trimester specific reference intervals for all thyroid function tests. The trimester specific ranges for TSH[5] are as follows:

- I trimester: 0.1to 2.5 mIU/L
- II trimester: 0.2 to 3.0 mIU/L
- III trimester : 0.3 to 3.0 mIU/L

Thyroid disorders during early pregnancy have been associated with adverse obstetric and fetal outcomes. The main obstetric complication are abortion, preeclampsia, placenta abruption, preterm labour. Fetal complications are impaired neuro-psychomotor development, reduced I.Q, prematurity, low birth weight ,stillbirth, neonatal hypothyroidism or hyperthyroidism depending on maternal thyroid status[5-7].Thyroid hormones play a critical role in fetal brain development. The fetus depends entirely on maternal thyroid hormones for the first 12 weeks of pregnancy, after which it begins to produce its hormones[8].Given that most common thyroid dysfunction that occur in pregnancy is subclinical hypothyroidism and lack of clear data for efficacy of treatment, there is ongoing debate regarding the need for universal screening for thyroid dysfunction during pregnancy[9-11].

As maternal thyroid disorders are quite prevalent ,easily diagnosed, and for which safe, effective treatment is available, some experts recommend universal screening for thyroid functions in I trimester[12]. While others support targeted screening and treatment of overt disease in pregnancy but oppose universal screening.With this background, the study was conducted in OBS & GYNAE

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department of Anugrah Narayan Magadh Medical College, Gaya to study the thyroid profile of first trimester pregnant women attending the OBG department and to evaluate whether thyroid function screening should be mandatory.

Methodology

The study was done on 200 first trimester pregnant women attending the Obstetrics & Gynaecology department of Anugrah Narayan(A N) Magadh Medical College & Hospital , Gaya from December 2014 to August 2016. A cross sectional study was done for thyroid profile of 200 pregnant women and to evaluate whether thyroid screening should be made mandatory or not. The study included apparently healthy I trimester pregnant women with singlet on pregnancy primigravida as well as multigravida and Pregnant women with multifetal gestation, with known thyroid disorders or medical illness like diabetes and hypertension, not willing were excluded.After consent from the study subjects and institutional ethics approval, detailed history was taken regarding the symptoms of thyroid disorders , obstetric history, menstrual history ,past medical history, family history, personal and social history. General examination was done with reference to the general condition of the patient, body temperature, pulse rate, blood pressure, respiratory rate and findings were recorded. Systemic examination of CVS,CNS, respiratory system and thyroid gland was done followed by per abdomen and per vaginal examination. Investigations included CBC,BT, CT, Blood grouping,RBS,HIV,HBSAg,Routine examination(R/E)of urine, USG (Ultrasonography).Pregnancy <12 weeks was confirmed by clinical assessment and USG.Pregnant patients fulfilling the inclus-ion criteria were enrolled in the study and sent for testing of serum TSH, fT4 and fT3.The reference ranges of test values used in the study were as per the guidelines of American Thyroid Association for Diagnosis and Management of Thyroid disease during pregnancy and postpartum[5]. As per the regulation 14.2 of American Thyroid Association guidelines, if trimester specific ranges for TSH are not available in the laboratory, the following reference ranges are recommended:

I trimester : 0.1 -2.5 mIU/L
II trimester : 0.2-3.0 mIU/L
III trimester : 0.3-3.0 mI U/L
Normal fT4 level is 0.7-1.8 ng /ml
Normal fT3 level is 1.7-4.2 pg/ml

Depending on the hormone values, patients were classified into:

- Subclinical Hypothyroidism: when TSH value is raised but FT3& FT4 values are normal
- Overt Hypothyroidism: When TSH value is raised , FT3 & FT4 values are lower
- Subclinical Hyperthyroidism: When TSH value is low but FT3 & FT4 values are normal
- Overt Hyperthyroidism: When TSH value is low , FT3 & FT4 values are raised

Results

Patients in our study were in the age range from 18 to 35 years. They were divided into four groups, 18-22 years (48.5%), 23-27 years (36%), 28-32 years (13%) and 33-35 years (2.5%) . Patients were distributed according to parity. In our study 96 (48%) cases were in P_0 (primipara) group, 60 (30%) cases in P_1 group, 28 (14%) patients were in P_2 group 14 (7%) patients were in P_3 group and 2 (1%) patients were in P4 group. 15 patients out of 96 cases of P_0, 9 patients out of 60 cases of P_1 and 2 patients out of 28 patients of P_2 had history of spontaneous abortion. 96 cases out of 200 belong to P_0 group (48%).Also P0group had the highest rate of history of spontaneous abortion 7.5% (15 Patients of 96). (Table 1)

Table 1: Distribution of cases according to Age, Parity

Age group	No of cases	Frequency	Parity	No. of cases	H/O spontaneous abortion
18-22YRS	97	48.50%	P0	96 (48%)	15 (7.5%)
23-27 YRS	72	36%	P1	60 (30%)	9 (4.5%)
32YRS	26	13%	P2	28 (14%)	2(1%)
33-35YRS	5	2.50%	P3	14 (7%)	-
Total	200	100%	P4	2 (1%)	-

The patients, were divided into four groups according their thyroid status subclinical hypothyroidism, subclinical hyperthyroidism, overt hypothyroidism and overt hyperthyroidism.In our study 71 (35.5%%) cases found to have subclinical hypothyroidism, 1(0.5%) case was found to have subclinical hyperthyroidism, 7 (3.5%) cases found to have overt hypothyroidism and 1 (0.5%) case was found to have overt hyperthyroidism.(Fig 1)

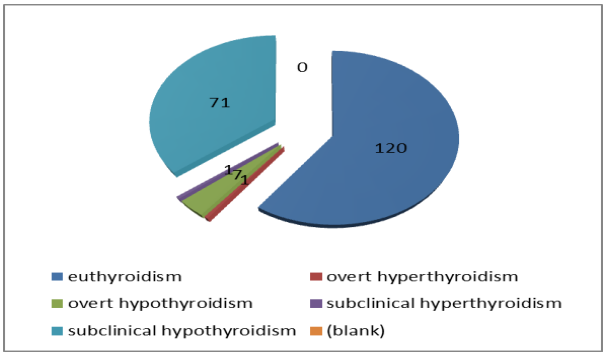

Fig 1:Thyroid Disorders in 200 women screened

The mean values of serum TSH in regard to thyroid function status are shown in table 2. In 71 cases of subclinical hypothyroidism the mean value was 4.38 mIU/L with SD of 1.45. In 1 case of subclinical hyperthyroidism the mean TSH value was 0.014 mIU/L. In 7 cases of overt hypothyroidism the mean value was 10.34 mIU/L with SD of 1.41. In 1 case of overt hyperthyroidism the mean TSH value was 0.02mIU/L .

We observed the following values of serum FT3 in our study . In cases of subclinical hypothyroidism the mean free T3 value was 4.06 pg/ml with SD of 0.59. In case of subclinical hyperthyroidism the

mean value was 4.6 pg/ml . In 7 cases of overt hypothyroidism the mean value was 1.51 pg/ml with SD of 0.41 and in 1 case of overt hyperthyroidism the mean value was 7.56 pg/ml.In 120 cases of euthyroidism ,the mean value was 3.96 pg/ml with SD of 0.57(Table 2)

Table 2:TSH,T3 and T4 Value Distribution In Different Thyroid Dysfunctions

Thyroid dysfunction	No. of cases	Mean TSH(mIU/l)	S.Deviation	Mean Serum FT3(pg/ml)	std deviation	Mean S.FT4(ng/dl)	Std. deviation
Subclinical hypothyroidism	71	4.38	1.45	4.06	0.59	1.22	0.24
overt hypothyroidism	7	10.34	1.41	1.51	0.41	0.46	0.14
Subclinical hyperthyroidism	1	0.014	-	4.6	-	1.4	-
Overt hyperthyroidism	1	0.02	-	7.56	-	4.3	-
Euthyroidism	120	1.52	0.63	3.96	0.57	1.24	0.28

We observed values of serum FT4 in our study. In 71 cases of subclinical hypothyroidism the mean value was 1.22ng/dl with SD of 0.24. In 1 case of subclinical hyperthyroidism the FT4 value was 1.40ng/dl. In 7 cases of overt hypothyroidism the mean value was 0.46 ng/dl with SD of 0.14 and in 1 case of overt hyperthyroidism the FT4 value was 4.30ng/dl. In 120 cases of euthyroidism , the mean FT4 value was 1.24 ng/dl with SD of 0.28(Table 2)

Table 3: Age Distribution of Thyroid Disorders

Age group(yrs)	Subclinical hypothyroidism	Overt hypothyroidism	Subclinical hyperthyroidism	Overt hyperthyroidism	Euthyroidism	P value
18-22	41	5	-	1	50	0.017
23-27	25	1	-	-	46	0.399
28-32	4	1	1	-	20	0.058
33-36	1	-	-	-	4	0.365
Total	71	7	1	1	120	

p<0.05 is significant.

Out of 71 cases having subclinical hypothyroidism, 66 (92.95%) patients were aged ≤ 27 yrs. Out of 7 cases having overt hypothyroidism, 6(85.7%) patients were aged ≤ 27 yrs. 1 case having overt hyperthyroidism was aged ≤ 27 yrs. 1 case having subclinical hypothyroidism was aged ≥ 27 yrs.Correlation between age and TSH (hypo and hyper) is p<0.05 positive correlation is significant only between 18-22 yrs of age.(Table 3)In our study the mean age of the study population is 23.50±3.80. Mean age for 71 cases of subclinical hypothyroidism was 22.49± 3.21 yrs. The mean age for 7 cases of overt hypothyroidism in our study was 22 ± 2.89 yrs. The mean age for 120 euthyroid cases was 24.16 ± 4.02 yrs. 1 case of subclinical hyperthyroidism was 29 yrs and that of overt hyperthyroidism was 20 yrs. in our study no relation was seen between thyroid status and age.(Fig 2)

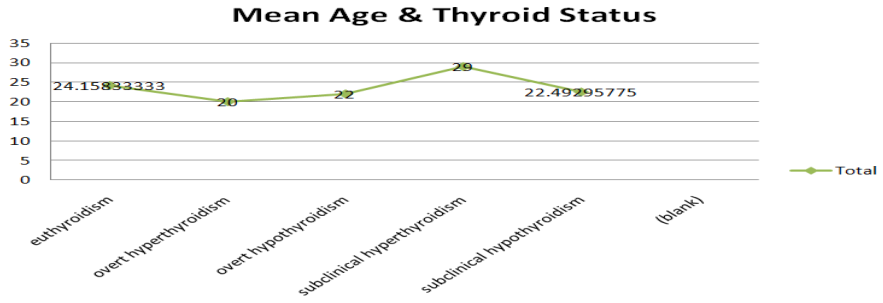

Fig 2: Mean Age in Relation to Thyroid Status

Table 4: Parity Distribution of Thyroid Disorders

Parity	Subclinical hypothyroidism	Overt hypothyroidism	Subclinical hyperthyroidism	Overt hyperthyroidism	Euthyroidism	P value
P0	48	6	-	1	41	0.00002
P1	10	1	-	-	49	0.00004
P2	10	-	1	-	17	0.9337
P3	3	-	-	-	11	0.142
P4	-	-	-	-	2	0.245
Total	71	7	1	1	120	

p<0.05 is significant

Out of 80 cases having thyroid disorders majority patients (67.5%.) were primiparous (P_0). Only 3 patients (3.75%) belonged to P_3 group.

There is statistically significant association between parity(P_0 & P_1) and prevalence of thyroid disorders as *p*-value is <0.05.
There is no statistically significant association between P2,P3& P4 and prevalence of thyroid disorders(Table 4)

Table 5: Showing History of Spontaneous Abortion in Thyroid Disorders

Thyroid status	Euthyroidism	Subclinical hypothyroidism	Overt hypothyroidism	Subclinical hyperthyroidism	Overt hyperthyroidism	Total
Total cases	120	71	7	1	1	200
h/o spontaneous abortion	6	16	4	0	0	26
		20				
Percentage	5%	22.5%	57.1%	0	0	13%
		25%				

Out of 200 patients, 26 patients gave history of previous spontaneous abortion in first trimester. 6 cases in euthyroid group (5%), 16 cases in subclinical hypothyroidism group (22.5%), 4 cases in overt hypothyroidism group (57.1%) had history of pregnancy loss. In our study only one case of subclinical hyperthyroidism and overt hyperthyroidism were screened and they had no previous history of spontaneous abortion.

There is a statistically significant increase in pregnancy loss in thyroid disorders as compared to the normal cases, with a *p*-value of <0.001.
We observed in our study that overt hypothyroids(57.1%.) and subclinical hypothyroids (22.5%%) were prone to have miscarriage which was significantly high.(Table 5,Fig3)

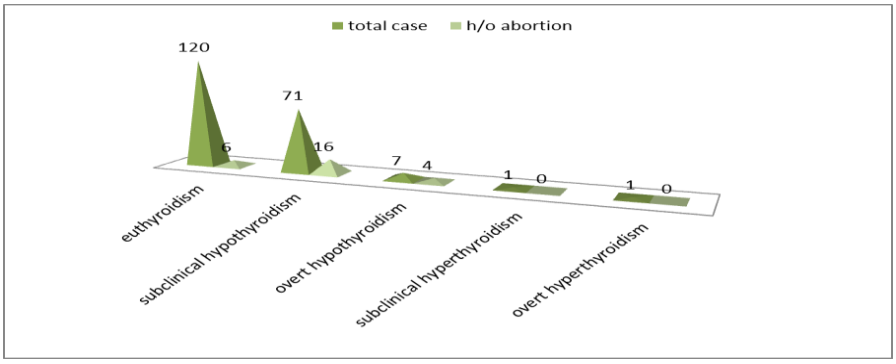

Fig 3:Showing relation of thyroid dysfunction with H/O spontaneous abortion

Discussion

Our study shows high cases of subclinical and overt hypothyroidism among pregnant women.Out of 200 women screened, 35.5% had subclinical hypothyroidism , 3.5 % had overt hypothyroidism, 0.5 % had subclinical hyperthyroidism and 0.5 % had overt hyper-thyroidism.The possible reason for high cases in our study was that we studied the individuals without high risk factors and we used the first trimester specific reference range.

Sahu, Meenakshi Titoria et al, screened 633 pregnant women in second trimester. TSH level estimated. If TSH level was deranged, then free T4 and thyroperoxidase antibody level were done. Patients were managed accordingly and followed till delivery. Their obstetrical and perinatal outcomes were noted. Their results showed that prevalence of thyroid dysfunction was high, with subclinical hypothyroidism in 6.47% and overt hypothyroidism in 4.58% women. Overt hypothyroids were prone to have pregnancy induced hypertension (P=0.04). IUGR (P=0.01) and intrauterine demise (P=0.0004) as compared to control. CS rate for fetal distress was significantly higher among pregnant subclinical hypothyroid women. (P=0.04). Neonatal complications and gestational diabetes were significantly more in overt hyperthyroidism group (P=0.03 and P= 0.04) respectively. They concluded that prevalence of thyroid disorders, especially overt and subclinical hypothyroidism (6.47%) was high. Significant adverse effect on maternal and fetal outcome were seen emphasizing the importance of routine antenatal thyroid screening[13].Vimal Nambiar et al. carried a study to establish the prevalence and the effect of thyroid dysfunction on pregnancy outcomes in Asian-Indian population. The study cohort comprised of 483 consecutive pregnant women in the first trimester attending the antenatal clinic of a tertiary center in Mumbai, India. Thyroid hormone levels and thyroid peroxidase antibody were estimated. Patients with thyroid dysfunction were assessed periodically or treated depending on the severity. Subjects were followed until delivery.

The study results was that the prevalence of hypothyroidism, Graves' disease,gestational transient thyrotoxicosis,and thyroid autoimmunity (TAI) was 4.8% , 0.6% , 6.4 % , and 12.4%, respectively.

Forty percent of the hypothyroid patients did not have any high-risk characteristics.

They concluded that the prevalence of hypothyroidism (4.8%) and TAI (12.4%) is high. TAI and hypothyroidism were significantly associated with miscarr-iage[14].In our study 71 cases of subclinical hypothyroidism mean value was 4.38 mIU/L with SD of 1.45. In 1 case of subclinical hyperthyroidism the mean TSH value was 0.014 mIU/L .

In 7 cases of overt hypothyroidism the mean value was 10.34 mIU/L with SD of 1.41. In 1 case of overt hyperthyroidism the mean TSH value was 0.02 mIU/L .These findings suggests that if we use nonpregnant TSH cut-off of 4.5 mIU/L rather than the first trimester specific TSH cut-off of 2.5 mIU/L than these cases would have been missed.Dosiou et al. supports universal screening of pregnant women as a cost-effective measure in various clinical scenarios. They

developed a model in which women were screened in the first trimester of pregnancy with TSH and anti TPO Ab. Women with TSH elevations underwent further testing, and treatment with LT4 was initiated when indicated. Their analysis showed that universal screening of pregnant women was a cost-effective measure compared to no screening at all[15].Dinesh K Dhanwal et al. conducted study on prevalence of subclinical hypothyroidism during first trimester of pregnancy in North India. A total of 1000 women were enrolled for this prospective observational study. The mean age of study subjects was 25.6 years, and mean gestational age was 10.3 weeks. One hundred and forty-three (14.3%) subjects had TSH values more than 4.5 mIU/L above the cut off used for definition of hypothyroidism. Out of these, 135 had normal free T4 and therefore labelled as subclinical hypothyroidism and 7 had low free T4 suggestive of overt hypothyroidism. TPO Ab was positive in 68 (6.82%) of total, 25 (18.5%) of subclinical and 5 (71%) of overt hypothyroid patients. They concluded that hypothyroidism, especially subclinical, is common in North Indian women during first trimester[16].Moreno Reyes et al. determine the prevalence of thyroid disorders in pregnant women in Belgium. The frequency of elevated serum TSH was 7.2%, indicating either subclinical hypothyroidism (6.8%) or overt hypothyroidism (0.4%). Among those women, 13.8% were thyroid peroxidase antibodies (TPO-Ab) positive. The frequency of low serum TSH was 4.1%, indicating either subclinical hyperthyroidism (3.6%) or overt hyperthyroidism (0.5%). In the entire population, the frequency of positive anti TPO-Ab positive women was 4%. Globally, the prevalence of thyroid disorders (abnormally high or low TSH) and thyroid autoimmunity features was 15.3% and 18.6% in first-trimester pregnant women[17].Gayatri et al. analyzed the prevalence of SCH among 495 pregnant women attending government hospital in South India. SCH was detected in 2.8%.Anti TPO antibodies were positive in 8.5% of the study population. Among the women with hypothyroidism, 57.1% have TPO antibody positive and among the euthyroid women 7.1 % had antibody positivity. In this study, SCH was defined as an asymptomatic state with normal FT4 and elevated TSH (5-10 mIU/L). This study showed that the prevalence of SCH among Indian pregnant women is fairly high and they have high rates of thyroid antibody positivity[18].Anupama Daveet al did the study to know the importance of universal screening for thyroid disorders in first trimester of pregnancy. In the 305 women screened mean age was 24.46 years, mean gestational age was 9.09 weeks,89.83% were euthyroid, 9.8% were hypothyroid, 0.32 % were hyperthyroid. Incidence of hypothyroidism in high risk population was 20.58% and in normal population was 6.7%. There was significant association of thyroid disorders with high risk factors ($P < 0.001$). In hypothyroid women 46% had adverse perinatal outcomes and 53.33% had normal outcomes. This shows statistically significant association abnormal TSH values with adverse pregnancy outcomes ($P < 0.001$). They conclude that there is significant correlation between risk factors and hypothyroidism. So high risk screening is mandatory in early pregnancy. But if we screen only high risk population we would miss 4.6% cases which could have been diagnosed and treated earlier[19]

Conclusion

In India, the prevalence of hypothyroidism in pregnancy is much higher compared to western countries. Prevalence varies widely among various states in India, as we still face iodine deficiency in many parts of the country. The most common cause of hypothyroidism in pregnancy in developing countries like India is iodine deficiency. In iodine sufficient areas, Hashimotos thyroiditis is the most common cause of hypothyroidism .

The presence of goiterogens in diet, micronutrient deficiency such as iron and selenium deficiency may cause hypothyroidism .Poverty ,insufficient iodine supplementation and fluorinated water may be the major cause for thyroid disorder among pregnant women. Heavy rainfall and floods may lead to decrease in iodine content in soil thus causing hypothyroidism.We conclude that despite great controversy over universal screening for thyroid function in pregnancy, high cases of thyroid disorders in Indian pregnant women makes it necessary to screen all the pregnant women in early pregnancy so that timely treatment can be given and fetal and maternal complications can be avoided.

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