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Dr. B Aruna Kumari
Associate Professor, Department of Gynaecology and Obstetrics, Modern Government Maternity Hospital, Petlaburz, Hyderabad, Telangana, India

Dr. A Suman Chandra
Professor, Department of Radiology Shadhan Medical College, Hyderabad, Telangana, India

Corresponding Author:
Dr. B Aruna Kumari
Associate Professor, Department of Gynaecology and Obstetrics, Modern Government Maternity Hospital, Petlaburz, Hyderabad, Telangana, India

Thyroid dysfunction during pregnancy in our experience

Dr. B Aruna Kumari and Dr. A Suman Chandra

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Abstract
Introduction: Women with known thyroid disease will need to have their treatment adjusted and more frequently monitored during pregnancy.
Aims: To determine the proportion of thyroid dysfunction in pregnancy and determine the different types of thyroid dysfunction during pregnancy.
Materials and Methods: The present study is an Observational Study done on 300 pregnant women with gestational age ≤14 weeks. It was done to detect the prevalence of thyroid dysfunction. TSH levels were evaluated in the subjects and if it was elevated, ft3 and ft4 was done. TPO antibodies was done in this with raised TSH, family history of thyroid disease and those with autoimmune disorders.
Results: The prevalence of thyroid disorders in the present study was 25%. The prevalence of hypothyroidism in the present study was 21.7%. The prevalence of subclinical hypothyroidism and overt hypothyroidism in our study was 16.7% and 5%. The prevalence of total hyperthyroidism was 3.3%. The prevalence of subclinical and overt hyperthyroidism in our study was 2.3% & 1% respectively. Among the hypothyroid, 22% of subclinical and 53.3% of overt hypothyroid were positive for TPO antibodies.
Conclusions: Serum TSH for all pregnant women will help in early detection, and by giving appropriate treatment it thus prevents maternal and fetal complications of thyroid disorders.

Keywords: Thyroid dysfunction, during pregnancy, experience

Introduction

Thyroid disease is the second most common endocrine disorder encountered in women of child bearing age after diabetes. The prevalence of hypothyroidism during pregnancy is 0.3-0.5% for overt hypothyroidism and 2-3% for subclinical hypothyroidism. Overall prevalence of hypothyroidism during pregnancy varies from 15.5% - 35.3% in South Americans. TPO positives were 12.4%. Gestational thyrotoxicosis was 6.5% and in the West it is 2-3%. It seems the prevalence of hypothyroidism is more in Asians.

Thyroid disorders are known to be associated with abnormal maternal and fetal outcomes and are often overlooked in pregnant women because of nonspecific symptoms and hyper metabolic state of pregnancy. The developing fetus synthesizes thyroid hormones only by the end of first trimester and hence depends on maternal hormones for organogenesis, general growth and development of central nervous system. Moreover thyroid hormones are essential for the maintenance and successful outcome of normal pregnancy. Pregnant women with thyroid dysfunction are at risk of pregnancy related complications like-spontaneous abortion, preeclampsia, abruption placenta, intrauterine growth restriction, preterm delivery, postpartum hemorrhage, low birth weight and still birth [3, 4].

The fetal effects of thyroid dysfunction during pregnancy are-lower scores of neuropsychological test related to intelligence, attention, language, reading ability, school performance and visual motor performance. Due to the high prevalence of thyroid dysfunction and its association with adverse pregnancy outcome, antenatal thyroid screening should be done. TSH as a routine screening at first antenatal visit is recommended so that the relevant thyroid disorder is corrected in time and to avoid adverse maternal and fetal outcome [4].

Estimation of serum TSH is a sensitive marker of thyroid dysfunction during pregnancy and has been suggested as a cost effective screening tool. This study is being conducted to determine the proportion and the types of thyroid dysfunction in pregnant women in our hospital.

Materials and Methods

It is a clinical study done in total of 300 pregnant women with gestational age ≤14 weeks who were screened for thyroid dysfunction initially with serum TSH. Study done in department of gynaecology and obstetrics as a part of screening for hypo or hyperthyroidism in pregnancy. After obtaining institutional ethical clearance subjects were selected as per inclusion and exclusion criteria.

Inclusion criteria

Pregnant women at risk for thyroid disorders as per American Thyroid Association. All high risk women such as known case of thyroid disorder hypothyroidism, hyperthyroidism, postpartum thyroiditis, thyroid lobectomy swelling of thyroid gland. Signs and symptoms, Family history of thyroid disease, thyroid autoantibody or other autoimmune disorder, History of head and neck irradiation, recurrent miscarriage, preterm delivery, infertility.

Exclusion criteria: Multiple gestation, Known case of hypertension, type 2 diabetes mellitus or other systemic disorders and Patient receiving medications which alter thyroid hormone.

Informed written consent from 300 pregnant women as per the inclusion criteria was selected. A detailed history was taken regarding the symptoms, and signs of thyroid disorders. Menstrual history, obstetric history, past history, medical history, family history and personal history was noted. A thorough general physical examination with reference to pulse, BP, temperature, respiratory rate were noted, followed by CVS, CNS, RS, per abdomen and local thyroid examination.

Along with routine antenatal investigation and obstetric scan, serum TSH will be done by chemiluminescent immunometric assay. TSH as per American Thyroid Association Guidelines trimester specific range will be considered.

1. If TSH was deranged fT3 and fT4 levels was checked.
2. Depending upon the FT3 and FT4 values they are grouped as subclinical or overt hypothyroidism or hyperthyroidism.
3. If they are subclinical/overt hypothyroid or had family history of thyroid disease or had history of autoimmune disease, then TPO antibodies was tested.
4. USG thyroid gland was done if thyroid gland was enlarged on clinical examination.
5. FNAC of the thyroid gland will be done if required.

Results

A total of 300 pregnant women with gestational age ≤14 weeks were screened for thyroid dysfunction initially with serum TSH. If Serum TSH was deranged then FT 3, FT 4 and TPO antibodies was done as per the methodology.

Table 1: Demographic distribution of patients studied.

Age in years	Number of patients	Percentages
< 19 yrs	2	0.7
20-24 yrs	130	43.3
25-29 yrs	121	40.3
30+yrs	47	15.7
Mean ± SD	25.41±3.73	
Locality of distribution		
Rural	110	36.7
Urban	190	63.3
Socio Economic Status		
Lower class	167	55.7
Middle class	133	44.3
Upper class	0	0
Gestational Age(weeks)		
<5weeks 6 days	17	5.7
6 weeks -7 6 days	81	27.0
8 weeks -9 weeks 6 days	72	24.0
10 weeks -11 weeks 6 days	51	17.00
12 weeks -14 weeks	79	26.3
Parity		
Primi	108	36.0
2nd Gravida	108	36.0
3rd Gravida	58	19.3
≥4th Gravida	26	8.7
BMI (kg/m²)		
<18.5	4	1.3
18.5-24.9	181	60.3
25-29.9	96	32.0
>30	19	6.3

Around 83.6% of the study population were between 20-29 yr with mean age of 25.41±3.73 yr. Around 63.3% of them belonged to urban locality. Around 55.7% of the study population belong to low socio economic status.

Around 73.7% of the women were screened for thyroid dysfunction in first trimester (<12 weeks) and 26.3% were between 12-14 weeks. 72% of the population were primi and second gravid, 8.7% were more than 4th gravid. Mean BMI was 24.84±3.30. Around 60.3% of the subjects had normal BMI. Mean BMI-24.84±3.30.

Table 2: Distribution of risk factors among the study population

Risk factors	Number of patients	Percentages
Obstetric risk factor		
H/O infertility	5	1.7%
Prenancy loss ≥2	7	2.3%
Past History		
k/c/o/ thyroid disease	13	4.3%
Goitre/irradiation of head and neck	0	0%
Family history of thyroid dysfunction	3	1%

2.3% of the study population had more than 2 abortions. 1.7% had history of taking treatment for infertility. 4.3% of the subjects had past history of hypothyroidism. 1% of the study population had a positive family history of thyroid dysfunction with all their mothers having been treated for hypothyroidism.

Table 3: Distribution of different values of serum TSH among the study population

Variables	Number of patients	Percentages
<0.1	10	3.3
0.1-2.5	228	76.0
2.6-5	40	13.3
5.1-7.4	8	2.7
7.5-10	10	3.3
>10	4	1.3
Ft3	75	
<2.5	22	7.3
2.6-4.4	50	16.7
>4.5	3	1.0
Ft4	75	
<12.2	29	9.7
12.3-21.3	41	13.7
>21.4	5	1.7

Mean S.TSH in the study population was 2.47±3.79. 76% had TSH between 0.1-2.5 IU/ml. 20.6% had TSH > 2.6IU/ml. Of these 1.3% had TSH more than 10mIU/ml. 16.7% had ft3 in the range of 2.6-4.4 pg/ml and 13.7% had ft4 between 12.3-21.3pmol/L.

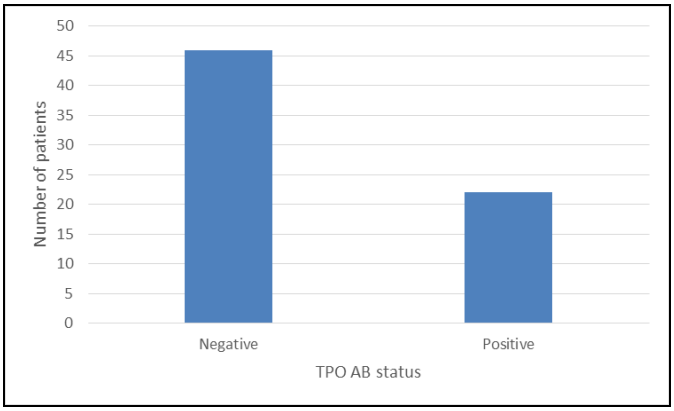

Fig 1: Presence of TPO AB among the patients studied

32.3% of the total hypothyroid, family h/o positive and with autoimmune disorders were positive for TPO antibodies.

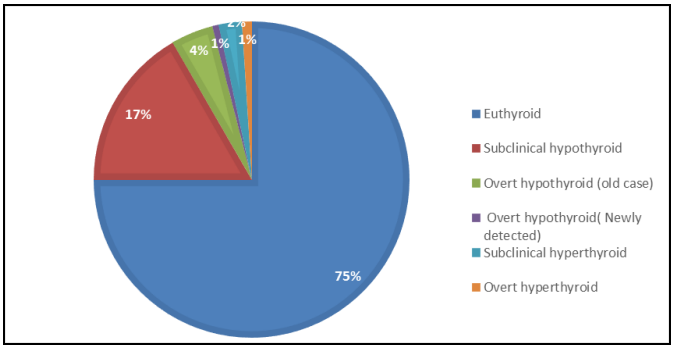

Fig 2: Distribution of study population as per their thyroid status

In the present study, total thyroid dysfunction was 25%. Among them 17% had subclinical hypothyroid, 5% had overt hypothyroid (of which 4% were k/c/o hypothyroid on treatment and 1% were newly detected hypothyroid), 2% had subclinical hyperthyroid and 1% had overt hyperthyroidism.

Table 4: Presence of TPO antibodies among women with thyroid dysfunction.

Thyroid Status	TPO AB		Total
	Negative	Positive	
Subclinical Hypothyroid	39(78%)	11(22%)	50(100%)
Overt Hypothyroid	7(46.6%)	8(53.3%)	15(100%)
Family h/o positive	3(100%)	0(0%)	3(100%)
History of autoimmune diseases	0(0%)	0(0%)	0(0%)

TPO antibody was positive in 22% of subclinical hypothyroid, 53.3% of overt hypothyroid. None of the subjects with family history of thyroid disease had positive TPO antibody.

Table 5: Parity and BMI distribution of patients studied in relation to Thyroid status

Parity	Thyroid Status					Total
	Euthyroid	Subclinical Hypothyroid	Overt hypothyroid	Subclinical hyperthyroid	Overt hyperthyroid	
Prime	78(34.7%)	20(40%)	5(33.3%)	4(57.1%)	1(33.3%)	108(36%)
2nd Gravida	86(38.2%)	15(30%)	5(33.3%)	2(28.6%)	0(0%)	108(36%)
3rd Gravida	42(18.7%)	8(16%)	5(33.3%)	1(14.3%)	2(66.7%)	58(19.3%)
>4th Gravida	19(8.4%)	7(14%)	0(0%)	0(0%)	0(0%)	26(8.7%)
Total	225(100%)	50(100%)	15(100%)	7(100%)	3(100%)	300(100%)
BMI (kg/m²)						
<18.5	3(1.3%)	1(2%)	0(0%)	0(0%)	0(0%)	4(1.3%)
18.5-24.9	138(61.3%)	30(60%)	4(26.7%)	7(100%)	2(66.7%)	181(60.3%)
25-29.9	67(29.8%)	17(34%)	11(73.3%)	0(0%)	1(33.3%)	96(32%)
>30	17(7.6%)	2(4%)	0(0%)	0(0%)	0(0%)	19(6.3%)
Total	225(100%)	50(100%)	15(100%)	7(100%)	3(100%)	300(100%)

P= 0.530, not significant, Fisher Exact test.
P value is not significant for distribution of subjects and hence parity has no effect on thyroid status in the present study.
P=0.104, not significant, Fisher Exact test

BMI in the present study has no significant effect on thyroid status. 73.3% of overt hypothyroid had BMI above the normal – between 25-29.9 kg/m².

Table 6: Clinical risk factor of patients studied in relation between different thyroid status and risk factors

Clinical risk factor	Thyroid status					Total (n=300)	P Value
	Euthyroid (n=225)	Schypo (n=50)	Overthypo (n=15)	Schyper (n=7)	Overthy Per(n=3)		
Infertility	3(1.3%)	1(2%)	1(6.7%)	0(0%)	0(0%)	5(1.7%)	0.619
H/o pregnancy loss of >2	3(1.3%)	3(6%)	1(6.7%)	0(0%)	0(0%)	7(2.3%)	0.248
Family history	1(0.4%)	1(2%)	1(6.7%)	0(0%)	0(0%)	3(1%)	0.187

Chi-Square test/Fisher Exact test
From the above table, family history of thyroid disease, obstetric risk factor had no effect on thyroid status.

Table 7: S.TSH distribution of patients studied in relation to Thyroid status

STSH	Thyroid status					Total
	Euthyroid	Schypo	Overthypo	Schyper	Overthyper	
<0.1	0(0%)	0(0%)	0(0%)	7(100%)	3(100%)	10(3,3%)
0.1-2.5	223(99.1%)	0(0%)	6(40%)	0(0%)	0(0%)	229(76.3%)
2.6-5	2(0.9%)	34(68%)	3(20%)	0(0%)	0(0%)	39(13%)
5.1-7.4	0(0%)	8(16%)	0(0%)	0(0%)	0(0%)	8(2.7%)
7.5-10	0(0%)	0(0%)	2(13.3%)	0(0%)	0(0%)	10(3.3%)
>10	0(0%)	0(0%)	4(26.7%)	0(0%)	0(0%)	4(1.3%)
Total	225(100%)	50(100%)	15(100%)	7(100%)	3(100%)	300(100%)

P<0.001**, significant, Fisher Exact test

68% of subclinical hypothyroid were in the range of 2.6-5mIU/ml. 40% of overt hypothyroid had TSH between 0.1-2.5 (13 cases were already known case of hypothyroid on treatment). All hyperthyroid patients had TSH below 0.1.

Statistical software
Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. The following assumptions on data is made,
+ Suggestive significance (P value: 0.05<P<0.10)
*Moderately significant (P value: 0.01<P≤0.05)
**Strongly significant (P value: P≤0.01)
The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 90.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

Discussion
Thyroid disease is the second most common endocrine disorder encountered in women of child bearing age after diabetes [5]. The prevalence of thyroid disorder is high in Asians. Thyroid dysfunction in pregnancy is associated with adverse maternal and fetal outcome. A total of 300 pregnant women with gestational age ≤14 weeks were screened for thyroid dysfunction.
In the present study the mean age was 25.41±3.73 yr, mean BMI was 24.84±3.30Kg/m² and around 72% were either primi and 2nd gravida. Most of them in the present study belong to lower and middle class and 63.3% were from urban area, this corresponds to that of the population attending our hospital which is situated in the heart of the city.
In the present study age, BMI, locality and socio economic status had no effect on thyroid status. In the study by Alpana Singh *et al*, there was no effect of BMI on different thyroid status [6]. In Ajmani *et al* study, most of the women with BMI > 24.58±1.5 had raised TSH [7]. In Dinesh *et al* study, there was no

correlation between socioeconomic status and thyroid status and they had women from both lower and middle class, which is similar to the present study [8].

In the present study we have also included pregnant women with previous history of thyroid disease who were already receiving treatment for it. Bijay Vaidya *et al* and Anupama D *et al* also included such cases in their study like the present study [8, 9]. There are few studies who have excluded such cases, such as those as those by Ajmani *et al*, Dinesh *et al* [7, 2].

A study by Tabia *et al* done in Israel showed that the incidence of thyroid dysfunction was 25.6% which is correlating to the present study, but as per Bijay Vaidya *et al* UK, study the prevalence of thyroid dysfunction was 4.5% which is lower than the present study [10, 8].

In Tabia *et al* study the incidence of hypothyroidism was 23.5% which is nearly correlating to the present study [10]. But as per Bijay Vaidya *et al*, a study from UK, hypothyroidism was 2.6%, which is much lower than the present study [8]. The present study had a prevalence of 21.6% of hypothyroidism which is correlating to Srinivas Rao and Anitha Patibandla study [11].

In Sapna C Shah the prevalence of hypothyroidism was 9% which does not correlate with present study [12].

The present study had a prevalence of 16.7% of subclinical hypothyroidism. In the study by Srinivas R and Anitha P the prevalence of subclinical hypothyroidism was 14.9% [11]. The present study nearly correlates with Srinivas Rao study.

In Sapna C Shah the prevalence of subclinical hypothyroidism was 5.3% which does not correlate with present study [12].

As from the above studies, prevalence of subclinical hypothyroidism is high in India. Hence it is important to screen all pregnant women for thyroid dysfunction.

The present study had 5% of overt hypothyroid. In the study by Srinivas R and Anitha P prevalence of overt hypothyroidism was 6.6% [11]. The present study nearly correlates with Srinivas Rao study. In a study by Sapna C Shah the prevalence of overt hypothyroidism was 2.7% which does not correlate with present study [12]. Though in the present study 4.3% were already known case of hypothyroidism on treatment, still these women came late for antenatal check up.

The present study shows a prevalence of hyperthyroidism of 3.3%. In a study by Tabia *et al*, the incidence of hyperthyroidism was 2.3% which is nearly correlating to the present study [10]. In a study by Bijay Vaidya *et al* the incidence of hyperthyroidism was 1.9% which is not correlating to the present study [8].

In Rajput R *et al* study, done in North India Haryana, showed prevalence of hyperthyroidism of 3.7%, which is consistent with the present study [13]. In study by Dinesh *et al* prevalence of hyperthyroidism was 0.3%, which is not consistent with the present study [2]. The present study shows a prevalence of 2.3% subclinical hyperthyroid. In R Rajput *et al* study, the prevalence o subclinical hyperthyroidism was 3.3%, which is consistent with the present study [13]. In Sapna C Shah the prevalence of subclinical hyperthyroidism was 1.32% which is also consistent with the present study [12]. The present study shows a prevalence of 1% were overt hyperthyroid. In Rajput R *et al* study, overt hyperthyroid were 0.4% and in Sapna C Shah study it was 0.7% which is consistent with the present study [12, 13].

Table 8: Prevalence of TPO antibody

Study	Total Hypothyroid	Subclinical hypothyroid	Overt hypothyroid	TPO positivity
Bijay Vaidya *et al*[8]			8 out of 16 overt hypo (50%)	8 out of 16 overt hypo (50%)
Dinesh *et al*[2] North India	-	18.5%	71%	18.5% of schypo and 71% of ovhypo
Ajmani[7]	52%	-	-	52% of total hypothyroid
Alpana S *et al* [6]	36.6%	-	-	36.6% of total hypothyroid
Das *et al*[14]	12.4%	-	-	12.4%
Present study	29.2%	22%	53.3%	29.2% of total hypo.22% of SChypo,53.3% of OVhypo

In the present study, TPO antibodies were positive in 22% of subclinical hypothyroid and 53.3% of overt hypothyroid. In Dinesh *et al* study, TPO antibodies were positive in 18.5% of subclinical hypothyroid and 71% of over hypothyroid, which was nearly correlating to the present study. In Das *et al* study, TPO was positive in 12.4% of total hypothyroid, in Alpana S *et al* study TPO antibody was positive in 12.4% of total hypothyroid, in Alpana S *et al* study TPO antibody was positive in 36.6% of total hypothyroid, where as in present study, it was present in 29.2% of total hypothyroid, where as in the present study, it was present in 29.2% of total hypothyroid patients, which is not correlating to the present study [6, 2, 13].

Draw back of the study are that we have used only serum TSH to know the prevalence of thyroid dysfunction and follow up of women with assessment of outcome has not been done.

Full thyroid evaluation with S.TSH, ft3, ft4 and TPO antibodies could n't be done for all women in view of cost. Ft3 and Ft4 have been done in those with deranged S.TSH. As the study period was for only one year, the maternal and fetal outcome could not be evaluated.

TPO antibodies have been done in those with raised S.TSH, family history of thyroid disease and in those with history of autoimmune disorders. Because presence or absence of TPO antibodies didn't change the management of cases, we have not done screening with TPO antibody as a routine in all cases. As per ITS, we have used serum TSH as the initial screening tool to detect thyroid dysfunction in pregnant women.

Conclusion

The Euthyroid status is important during first and second trimester of pregnancy for optimal fetal neuronal development. Suboptional maternal thyroid functioning indicated by high TSH has detrimental effects on the fetal brain development and IQ. Thyroid diseases have multiple deleterious impacts on pregnancy, postpartum and developing fetus. Hence prenatal screening with serum TSH in early pregnancy is important for good pregnancy outcome. The prevalence of hypothyroidism is more in Asians as compared to the West. Thyroid disorders are known have adverse maternal and fetal outcomes. Due to the high prevalence of thyroid dysfunction in the present study, doing S.TSH for all pregnant women will help in early detection, and by giving appropriate treatment it thus prevents maternal and fetal complications of thyroid disorders. TPO antibodies are a marker for an increased risk of infertility, miscarriage, preterm delivery and development of postpartum thyroiditis. Doing serum TSH is cost effective and can be used

as a first line screening method to detect thyroid dysfunction in pregnancy.

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