A retrospective study of effect of thyroid disorders on obstetric and perinatal outcomes: A hospital based study

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Abstract

Aims and Objectives: The study was undertaken in pregnant women to understand and analyze the obstetric and fetal outcomes of thyroid disorders.

Materials and Methods: TSH estimation was used as universal screening in their first visit to our hospital. Those patients with abnormal TSH values, i.e. above 2.5mIU/ml in first trimester and above 3mIU/ml in second and third trimesters were evaluated for freeT3, freeT4 and TPO Abs. They were treated accordingly and dosage adjustments made and the tests repeated once in 4-6 weeks. They were followed throughout pregnancy and delivery.

Results: Total no of pregnant women screened were 860, of which 130 had abnormal thyroid functions, thereby the prevalence of thyroid disorders being 15.11%. Of the 130 patients with thyroid disorders, 126 were hypothyroid and 4 were hyperthyroid. Among the 126 hypothyroid cases, 48 were known cases and 78 were new cases. The total cases of subclinical hypothyroidism were 91, prevalence being 10.58% and overt cases were 35, prevalence being 4.06%; 4 cases were overt hyperthyroid, prevalence being 0.4%. 60.3% of subclinical hypothyroidism were TPO positive and 39.6% of overt hypothyroidism were TPO positive (p value-<0.05). Out of 130 abnormal thyroid function patients, 98 patients delivered in our hospital. There were 16 abortions, 14 spontaneous and 2 terminations of pregnancies; 6 patients were lost for follow up, 7 patients have delivered outside and 1 patient lost follow up.

Conclusions: The prevalence of thyroid disorders during pregnancy was significantly more in our study, hypothyroidism being the commonest.

Significant numbers of cases were newly diagnosed on universal screening. The commonest disorder was subclinical hypothyroidism. Adverse maternal and fetal outcomes were almost similar in both subclinical and overt hypothyroidism. The common adverse outcomes noted were abortions, pre-eclampsia, gestational diabetes mellitus, preterm births and increased rates of caesarean sections. The adverse outcomes were significantly more in autoimmune antibody positive patients.

Keywords: Sub-clinical hypothyroidism, Overt hypothyroidism, Thyro peroxidase antibody (TPO Abs), Hyperthyroidism, preterm abortions, IUGR, Eclampsia.

Introduction

The thyroid gland is a small endocrine organ located in front of the trachea which utilizes iodine to produce thyroid hormones, which are essential for normal growth, development, maturation and regulation of metabolism. Over the past several years it has been proved that maternal thyroid disorders influence the outcome of mother and fetus, during and also after pregnancy.

Thyroid diseases are known to affect the reproductive health of women, who thus have trouble in conceiving or have more miscarriages.[1,2]

Thyroid dysfunction has a relatively high prevalence during pregnancy, affecting upto 5% of all pregnant women.[3] The most frequent thyroid disorder in pregnancy is maternal hypothyroidism. It is associated with fetal loss, fetal growth restriction, placental abruptions, pre-eclampsia, preterm delivery and reduced intellectual function in the offspring.

Autoimmune positive hypothyroid pregnancy shows doubling of incidence of miscarriage and preterm delivery.

The most serious effect of thyroid dysfunction on the developing fetus is decreased intelligence quotient of the offspring.[4,5] The fetus is totally dependent on maternal thyroid hormone supply during the first trimester of pregnancy, which is the important time in organogenesis.[6] As thyroxin is essential for fetal neurodevelopment, it is critical that maternal delivery of thyroxin to the fetus is ensured early in gestation.

So the key is to correctly identify these disorders and appropriately treat them to prevent pregnancy related complications and to ensure delivery of a healthy baby.

Aims and Objectives of the Study

1. To calculate the prevalence of thyroid disorders during pregnancy in a hospital based pregnant population.
2. To know the type of thyroid disorders in these subjects.
3. To assess the obstetric and perinatal outcome in these subjects.

Materials and Methods

Source of Data: Department of Women and Child Health, Narayana Health Multispeciality hospital.

Study Population: Pregnant women in any trimester of pregnancy who attended the outpatient department, inpatient department and the labour ward of OBG, NHMSH for the first time over a period of one year were selected for the study and were followed up till delivery and the perinatal period.

Inclusion Criteria

1. All pregnant women belonging to any trimester of pregnancy who reported to the obstetric department of NH-MSH were studied retrospectively.
2. Pregnant women with established thyroid dysfunction with or without treatment in any trimester of pregnancy were also studied for obstetric and perinatal outcome.
3. The high risk group including patients with current medical h/o autoimmune disorders or family h/o thyroid diseases were also included.

Exclusion Criteria: Women on drugs inflencing thyroid functions like Lithium, Iodine, Amiodarone, etc.

Complete history was taken and detailed examination was performed on the patient according to the proforma. Informed consent to participate in this study was taken. Serum samples were collected for TSH estimation by chemiluminescence immunoassay technique in our laboratory. When TSH was abnormal, free T4, free T3 and anti TPO antibodies were estimated. Women diagnosed with abnormal hormone levels were referred to endocrinology clinic of our institution for a simultaneous treatment and follow up. Routine antepartum management was done and women were followed till delivery and perinatal period.

Normal readings of our laboratory standards:
TSH values
First trimester: 0.1-2.5mIU/ml
Second trimester: 0.2-3.0mIU/ml
Third trimester: 0.3- 3.0mIU/ml
Free T3 values- 2.0-3.8 pg/ml
Free T4 values- 0.72- 2.24ng/dl

Maternal outcome variables included the occurrence of abortions, pre-eclampsia, gestational diabetes mellitus and obstetric complications like abruptio placenta, overall rate of caesarean sections, assisted vaginal delivery.

Perinatal outcome variables included the incidence of LBW, prematurity, IUGR, fetal demise and congenital hypothyroidism.

Statistical Methods

Statistical tools: The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of a computer using SPSS version 17.

Chi square test was used to analyze the differences between the proportions (comparative groups), wherever applicable.

A 'p 'value less than 0.05 was taken to denote a significant relationship.

Interpretation of 'p 'values
Suggestive significance: $0.05<p<0.10$
Moderately significant: $0.01<p<0.05$
Strongly significant: $p<0.01$

Results

In this study, a total of 860 pregnant patients were screened for the thyroid functions. Out of the 860 pregnant patients, 130 of them had abnormal thyroid functions.

Prevalence of thyroid disorders during pregnancy- 15.11%.

The mean age of the patients screened was 27.2 years.

1. Out of the 130 cases, 56 were primigravidae and the remaining 74 were multigravidae. Among the multigravidae, 46 were second gravidae, 21 were third gravidae and remaining 07 were higher order gravidae.
2. At the beginning of the study, 50 cases (only 38.5%) were known cases of thyroid dysfunction, of which known cases of hypothyroidism were 48 (36.9%) and known cases of hyperthyroidism were 02 (1.53%) cases. The remaining 80 cases (61.5%) were newly diagnosed during screening. Of the 80 new cases, 78 were hypothyroidism (60%) and 2 were hyperthyroidism cases (1.53%).

Table 1: Distribution of thyroid cases

	Frequency	Percent
Known hypothyroid	48	36.9
Known hyperthyroid	02	1.5
New hypothyroid	78	60
New hyperthyroid	02	1.5
Total	130	100

Of the 126 hypothyroid cases, 91 cases (72.22%) were subclinical hypothyroidism and 35(27.77%) were overt hypothyroidism cases.

Of the 4 hyperthyroid cases, all were overt hyperthyroidism cases and there were no subclinical hyperthyroid cases.

Table 2: Distribution of hypothyroid and hyperthyroid cases

	Frequency	Percent
Subclinical hypothyroidism	91	70
Overt hypothyroidism	35	26.9
Overt hyperthyroidism	04	3.1
Total	130	100

Of the 126 hypothyroid cases, 53 cases (42%) were TPO positive and 73 (57.9%) were TPO negative.

Table 3: Distribution of TPO positive and negative cases

	Frequency	Percent
TPO Negative	73	57.9
TPO Positive	53	42.1
Total	126	100

Of the 53 TPO positive cases, 32 cases (60.3%) were subclinical (euthyroid) TPO positive cases and 21 cases (39.6%) were overt TPO positive cases. Of the 73 TPO negative cases, 59 cases were subclinical cases and 14 cases were overt cases. So:

TPO Positivity among subclinical hypothyroidism- 60.3%

TPO Positivity among overt hypothyroidism- 39.6%

The Chi square value is 8.956 (p value< 0.05) and hence the association between hypothyroidism and TPO positivity is statistically significant.

Of the total 130 cases of thyroid disorders, there were 16 abortions. Of the remaining 114 cases, 98 patients delivered in our hospital, 8 patients were lost for follow up, 8 patients have delivered outside.

The fetal outcome in the 98 cases were as follows: There were 76 normal fetuses and 22 abnormal fetuses. Abnormal fetuses included preterm, IUGR, LBW and IUD babies. Among the 22 abnormal fetuses, 14 were preterm, 2 were IUDs and the remaining 6 included IUGR, LBW and SGA babies.

The two IUDs were seen in subclinical TPO positive hypothyroid cases. 1 was due to pre eclampsia with abruption. The other had severe IUGR and landed up in IUD at 30 weeks.

The correlation between diagnosis and fetal outcome are as follows:

Table 4: Fetal outcomes in thyroid disorders
Diagnosis * Foetus cross tabulation

Count		Foetus		Total
		Normal	Abnormal	
Diagnosis	Sub-clinical Hypothyroidism	58	12	70
	Overt Hypothyroidism	16	10	26
	Overt Hyperthyroidism	2	0	2
Total		76	22	98

The chi square value is 5.691 and so the p value is <0.05 and so the association between thyroid disorders and abnormal fetal outcome is statistically significant.

The association between TPO antibodies and fetal outcome are as follows:

Table 5: Fetal outcomes in TPO positivity

TPO abs * Foetus Cross tabulation				
Count		Foetus		Total
		Normal	Abnormal	
TPO abs	TPO-Negative	60	3	63
	TPO-Positive	16	19	35
Total		76	22	98

The chi square value is 30.89 and so the p value is <0.05 and so the association between TPO positivity and abnormal fetal outcome is statistically significant.

The adverse obstetric and perinatal outcomes associated with thyroid disorders during pregnancy are as follows.

Table 6: Obstetric and perinatal outcomes in thyroid disorders

Complications	Hypothyroidism	Hyperthyroidism
Abortions	15(11.9%)	01(25%)
Pre eclampsia	18(14.28%)	02(50%)
GDM	10(7.93%)	01(25%)
Pre-eclampsia + GDM	05(3.9%)	01(25%)
PPROM	04(3.2%)	00
Preterm births	14(11.11%)	02
IUGR/ LBW	08(6.3%)	00
Abruption	01	01(25%)
Stillbirth / IUD	02	00

There was overlapping of complications like Pre eclampsia, GDM, preterm births, IUGR and abruption in some cases.

In our study, there were 16 abortions (12.3%). 14 were spontaneous and 2 were terminated in view of high TSH levels (>150mIU/ml) and strong TPO positivity (>1500). Of the 16 abortions, 14 were in TPO positive cases and only 1 in TPO negative case. 1 abortion was seen in hyperthyroidism.

Prevalence of abortions in thyroid dysfunction- 12.3%.

Prevalence of abortions in TPO+ve cases- 26.41%.

There were 20 cases of pre eclampsia, 15 in TPO +ve patients, 3 in TPO –ve cases and 2 in hyperthyroid patients.

Prevalence of pre eclampsia in thyroid dysfunction-15.38%.

Prevalence of pre eclampsia in TPO +ve cases-28.3%.

There were 11 cases of GDM, 7 in TPO +ve, 3 in TPO –ve and 1 in hyperthyroidism.

Prevalence of GDM in thyroid dysfunction-8.46%.

Prevalence of GDM in TPO +ve cases- 13.2%

There were 6 cases who had both pre eclampsia and GDM and among them, 5 were in TPO +ve and 1 was in hyperthyroidism. Prevalence of pre eclampsia and GDM in TPO +ve cases- 9.43%.

No case of congenital hypothyroidism was seen among the babies.

Discussion

According to our study, the prevalence and pattern of thyroid disorders during pregnancy were as follows:

1. Prevalence of thyroid dysfunction during pregnancy- 15.11%.
2. Subclinical hypothyroidism- 10.58%.
3. Overt hypothyroidism- 4.06%.
4. Hyperthyroidism- 0.4%.

In our study, we observed that the prevalence of thyroid disorders during pregnancy was significantly more. Hypothyroidism was more common than hyperthyroidism.

Newly diagnosed cases of thyroid dysfunction by universal screening using TSH were significant in numbers, the commonest disorder being subclinical hypothyroidism. Adverse maternal and fetal outcomes were almost same in both subclinical and overt hypothyroidism. The common adverse outcomes noted were abortions, pre-eclampsia, gestational diabetes mellitus, preterm births and increased rates of caesarean sections. The adverse outcomes were significantly more in autoimmune antibody positive patients.

Most of the western literature say that the prevalence of subclinical hypothyroidism is 2- 2.5% and the prevalence of overt hypothyroidism is 2-3/1000 pregnant population.

Vanderpump and Turnbridge[7] reported a prevalence of 1-2% for overt hypothyroidism and 8% for subclinical hypothyroidism.

One Indian study done by Sahu et al[8] studied 633 patients in second trimester and found the prevalence of SCH to be 6.47% and OH to be 4.58%.

The prevalence rates in our study were comparatively higher probably because our cut off values for TSH were gestational age specific, 0.1-2.5mIU/ml, 0.2-3.0mIU/ml, 0.3-3.0mIU/ml for first, second and third trimesters respectively. The cut off value in the study by Sahu et al was 0.5-5.5mIU/ml. The upper limits of normal TSH reference ranges used to define SCH differed between the studies (range 2.5–6 mIU/L). These methodological differences potentially have a major bearing on the prevalence.

Also, in our study, those patients who were already known cases of thyroid disorders with or without treatment were also included whereas they were excluded in the study by Sahu et al.

Non-pregnant TSH reference values are unreliable in pregnancy. The TSH reference value in our study was between 0.1-3.0mIU/ml. This was adapted because it is supported by literature.

Serum TSH>2.5mIU/ml in first trimester shows T4insufficiency- Spencer et al.[9]

Biological reference value of TSH is 0.5-1.5mIU/ml- Cleveland clinic Journal of Medicine, 2002.[10]

American Thyroid Association[11] has stressed daily dosage of thyroxine should be adjusted to keep TSH at 1-2mIU/ml.

Truly normal range of TSH is defined as 0.5-2.5mIU/ml- William et al.[12]

Individuals with >2mIU/ml of TSH have a higher incidence of later hypothyroidism.[12]

Also in our study, we employed universal screening of thyroid dysfunction during pregnancy. Targeted case finding is recommended at the first prenatal visit or at diagnosis of pregnancy. Vaidya et al[13] recently reported a study of screening by means of TSH, T4, free T4, and TPO-Ab in 1560 consecutive pregnant women. An important result was that screening only women considered "high risk" on the basis of a personal or family history of thyroid disease, or a history of other autoimmune disease, would have missed 30% of women with overt or SCH.

A large-scale double-blind prospective study, entitled the "Controlled Antenatal Thyroid Screening Study," has been initiated by Lazarus and associates. Serum samples are obtained before 16 wk gestation, with half of the sera analyzed immediately for free T4 and TSH, and the other half frozen until delivery. Women with a free T4 below the 2.5th percentile and/or TSH above the 97.5th percentile receive levothyroxine therapy. The main outcome measure will be the development of the unborn child as measured at 3 year of age. Outcome data, when available, will be instrumental in beginning to develop a rational response to the screening controversy.

Prevalence of anti TPO antibodies

In our study, the prevalence of anti TPO antibodies are as follows:

1. Overall, TPO positivity among hypothyroid patients- 42.1%.
2. TPO Positivity among subclinical hypothyroidism-60.3%.
3. TPO Positivity among overt hypothyroidism-39.6%.

The Chi square value is 8.956 (p value< 0.05) and hence the association between hypothyroidism and TPO positivity is statistically significant.

In a prospective population study of 9471 pregnant women in the United States in whom serum TSH was measured during the second trimester, hypothyroidism was diagnosed in 2.2% of the cohort and autoimmune thyroiditis was present in 55% of women with SCH and more than 80% in women with OH.[14]

90% of women with hypothyroidism during pregnancy test positive for thyroid antibodies.[15]

A thyroid autoantibody prevalence of up to 15% has been found in pregnant populations.[16]

Again the difference in the prevalence rates could be due to the cut off value for TPO positivity used which was 60 in our study and varies from 60-143 in various studies.

Obstetric and perinatal outcomes

The overall rate of miscarriage is 12.3% (p value< 0.05) in our study but the majority occurred in TPO positive cases. More than 26.4% abortions were in the TPO positive group.

Hypothyroid women in particular have high miscarriage rates: in hospital material 67% of inadequately treated hypothyroid women miscarried.[2]

In one study, in which hospital ambulatory patients were evaluated, even women with mild subclinical hypothyroidism (TSH 2.5–5 mIU/L in TPO-Ab-negative women) had higher, almost double, rates of pregnancy loss compared with euthyroid women.[17]

In contrast, in a prospective population-based study, no increase in miscarriage rate was seen among those with clear-cut subclinical hypothyroidism (TSH > 4.29 mU/L).

Women with mild subclinical hypothyroidism (TSH ≥ 2.5mU/L) and pregnancy achieved by way of in-vitro fertilization showed no increase in miscarriage rate (13% *vs.* 13% in euthyroid women) or difference in pregnancy rate compared with euthyroid women.[18]

Differences between studies may be connected to the populations involved. The studies are of highly different characters and those based in hospital settings probably represent populations more susceptible to adverse outcomes.

Our study noted more than 25% abortions were in the TPO positive group.

In a study conducted by Stagnaro-Green et al**[1]** 552 women were screened in the first trimester of pregnancy for thyroid antibodies. He found that women who were thyroid antibody positive miscarried at a rate of 17% compared with 8.4% for the autoantibody-negative women.

Glinoer et al[19] in their study examined 120 euthyroid pregnant women for thyroid abnormality and found that one group (n=45) was positive for thyroid autoantibodies. This group had an increased risk of spontaneous abortion (13% vs. 3%).

A prospective, randomized trial conducted by Negro et al,[20] involved 984 women who were screened for TPO-Ab positivity and thyroid function tests at the first obstetrical visit. 115 women who were TPO-positive were divided into two groups: Group A (n = 57) included TPO women treated with levothyroxine; Group B (n = 58) included TPO women who received no levothyroxine intervention. Group C (n = 869) included all TPO antibody-negative women, none of whom received levothyroxine. Outcome parameters included spontaneous pregnancy loss and preterm delivery (delivery before 37 wk gestation). The abortion rate was significantly higher in Group B (13.8%) than in Group A (3.5%) or C (2.4%) (p <0.05). Similarly, the preterm delivery rate was higher in Group B (22.4%) than in Group A (7%) or C (8.2%) (p < 0.05).

So the prevalence of abortions in our study matched the literature.

In our study, the adverse maternal and fetal outcomes seen were predominantly pre-eclampsia (p value<0.01), gestational diabetes (p value <0.05), preterm births (p value <0.05) and to a small extent IUGR and IUDs. There was a significant overlap of pre eclampsia and gestational diabetes and preterm births. The overall rates of caesarean sections (p value <0.05) was also high in patients with thyroid disorders. LSCS rates were higher in thyroid disorders because of associated complications like pre eclampsia, gestational diabetes, IUGR, etc. The chi square value is 5.691 and so the p value is <0.05 and so the association between thyroid disorders and abnormal fetal outcome is statistically significant.

Also it was seen that all these complications occurred at significantly high rates in women with TPO positivity. The chi square value was 30.89 and so the p value is <0.05 and so the association between TPO positivity and abnormal fetal outcome is statistically significant.

In a study done by Leung et al[21] about the perinatal outcome in 68 hypothyroid patients, 23 with OH and 45 with SCH found that gestational hypertension was significantly more common in women with OH (22%) and SCH (15%) than in the control population (8%). The low birth weights observed in both women with OH and SCH was secondary to premature delivery due to gestational hypertension. The findings in our study was relevant with that of the literature.

Among the hyperthyroid patients, 1 patient had abortion, 1 patient had pre-eclampsia and abruption and 1 patient had only pre eclampsia and 1 patient was lost for follow up.

Sahu et al conducted a similar study in 633 patients and concluded that overt hypothyroids are prone to have pre eclampsia, intra uterine growth restriction, intrauterine demise as compared to control. Also the overall caesarean section rates for fetal distress is significantly high in subclinical hypothyroid pregnant women. Neonatal complications and gestational

diabetes is comparatively higher in overt hyperthyroid cases.

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