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Original Research Article

The effect of thyroid disorders on obstetric and perinatal outcomes: an observational retrospective study in a tertiary care center of north India

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ABSTRACT

Background: The incidence of hypothyroidism in pregnancy is between 0.5-3.5%, hyperthyroidism occurs in about 0.2-0.4%. They are associated with various maternal-fetal complications.
Methods: This retrospective observational cohort study was conducted in SMGS Hospital, Jammu, India after ethical clearance. Admitted patients were included over a period of 1 year from January to December 2021. Inclusion criteria was women belonging to any period of gestation admitted to the labour room and woman with established thyroid disorder. Exclusion criteria was women on drugs influencing thyroid functions.
Results: 1641 (10.43%) of 15722 women had thyroid disorders. Hypothyroidism in 10.37% (8.99% subclinical and 1.37% overt) and hyperthyroidism in 0.06%. PPROM was seen in 5.9% subclinical, 2.7% overt hypothyroid, none of hyperthyroid group. 7% subclinical, 8.5% overt hypothyroid and 1/10 women in hyperthyroid group had GDM. Abruption seen in 2.5% subclinical, 1.7% overt hypothyroid and none in hyperthyroid. In subclinical group 3.2% had gestational hypertension, 5.2% had preeclampsia and 0.6% had eclampsia. In overt hypothyroid, 2.8% had gestational hypertension, 7.9% preeclampsia and 1.7% eclampsia. In hyperthyroid group, 1/10 had gestational hypertension, 1/10 had preeclampsia. 18.2% subclinical, 14.7% overt hypothyroid, 2/10 in hyperthyroid group had history of abortion. 7% subclinical, 9.6% overt hypothyroid and 0/10 hyperthyroid group had infertility. 25.8% babies born were abnormal in terms of less gestational age at birth, low birth weight, IUGR, low apgar and IUD. 16.5% babies that had low birth weight <2.5 kg.
Conclusions: The impact of thyroid disorders warrants routine screening for thyroid dysfunctions in all women in prenatal and antenatal period to predict and prevent adverse maternal-neonatal outcomes.

Keywords: Hyperthyroidism, Hypothyroidism, Pregnancy, Thyroid disorders

INTRODUCTION

The thyroid, is a butterfly shaped endocrine gland that undergoes considerable glandular hyperplasia and increased vascularity in pregnancy. Thyroid diseases are the second most common endocrine disorders affecting women in the reproductive period, after diabetes.[1]

A large plasma volume and thus an altered distribution of thyroid hormone, increased thyroid hormone metabolism, increased renal clearance of iodide, and higher levels of hepatic production of thyroxine-binding globulin (TBG) in the hyperestrogenic state of pregnancy are responsible for higher thyroxine requirements in pregnancy.[2]

The incidence of hypothyroidism in pregnancy is between 0.5-3.5% whereas hyperthyroidism occurs in about 0.2-0.4%.

Thyroid disorders are associated with premature birth, fetal cardiac complications, low birth weight, increased frequency of cesarean delivery, placental complications,

preeclampsia and gestational hypertension, perinatal morbidity-mortality, and cognitive dysfunction, stillbirth, abortion, premature birth, heart failure and even thyroid storm.[3]

Early diagnosis and treatment of thyroid diseases before and during pregnancy is important for maintaining the health of the mother and the baby.

Objectives

Objectives of the study were to assess maternal outcomes in thyroid disorder and to assess perinatal outcomes in thyroid disorder.

METHODS

This retrospective observational cohort study was conducted in SMGS Hospital, Jammu, Jammu and Kashmir, India. Admitted patients were included over a period of one year from January 2021 to December 2021.

Inclusion criteria

Pregnant women belonging to any period of gestation admitted to the labour room. Pregnant woman with established thyroid disorder, either with or without treatment.

Exclusion criteria

Pregnant women on drugs influencing thyroid functions like lithium, iodine, amiodarone.

Hypothyroidism was diagnosed by trimester specific TSH levels as recommended by FOGSI thyroid dysfunction in pregnancy guidelines 2019- 1st trimester: 2.5 mIU/ml, 2nd trimester: 3 mIU/ml and 3rd trimester: 3 mIU/ml. Levels above them was grouped as hypothyroid. Serum total T_4 levels were used to categorize them as either overt (TT_4 less than the normal range as specified by laboratory) or subclinical (TT_4 within the lab specified range). Hyperthyroidism was diagnosed with decreased TSH values, further as subclinical if the FT_4 and/or FT_3 in the normal range, or overt if FT_3 or FT_4 were increased which was as per FOGSI thyroid update in pregnancy January 2021.

Patients data was collected from the records with hospital medical records department, including detailed history, examination, investigations including thyroid function tests, delivery notes and course of hospital stay.

Maternal outcomes studied were the occurrence of abortions, gestation hypertension, pre-eclampsia, gestational diabetes mellitus, abruption placenta, overall rate of caesarean sections and vaginal delivery.

Perinatal outcomes studied were the incidence of low birth weight, IUGR and fetal demise.

Statistical analysis

The information collected regarding all the selected cases were recorded in a master chart. Data analysis was done with the help of a computer software SPSS version 20.0. Each adverse obstetric and perinatal outcome was assessed separately. The qualitative data was represented as percentage. Quantitative data was analysed by mean, standard deviation. The association between two qualitative data was analyzed by chi-square test and P value <0.05 was considered significant.

RESULTS

In our study there were 1641 of 15722 patients with thyroid disease, comprising of 10.43% of admitted women. Hypothyroidism was prevalent in 10.37% of women and hyperthyroidism in 0.06%. Out of the 1384 women admitted with abortion, 164 (11.8%) had thyroid disorders.

Table 1: Type of thyroid disorder.

Type of thyroid disorder	No. of patients	Percentage
Subclinical hypothyroidism	1153	86.14
Overt hypothyroidism	176	13.10
Hyperthyroidism	10	0.74
Total	1339	100

The 1339 out of the 1641 who delivered in the hospital were further analysed for maternal and fetal outcomes. The type of thyroid disorders is tabulated in Table 1.

The population dynamics was almost similar in all three categories. Their mean ages were 26.3, 25.8 and 26.1 years in subclinical hypothyroidism, overt hypothyroidism and hyperthyroidism group respectively (Table 2).

Table 2: Demographic characteristics (expressed as mean±standard deviation).

Population dynamics	Subclinical hypothyroidism	Overt hypothyroidism	Hyperthyroidism
Age (years)	26.3±4.07	25.8±3.83	26.1±3.47
Gravidity	1.8±0.92	1.7±0.84	1.6±0.91
Previous abortions	1.2±0.61	1.1±0.60	1±0.0
Period of gestation	37.9±2.15 weeks	38.0±1.81 weeks	37.2±2.85 weeks

Table 3: Obstetrical conditions.

Obstetrical events	Subclinical hypothyroid N (%)	Overt hypothyroid N (%)	P value	Hypothyroid N (%)	Hyperthyroid N (%)	P value
PPROM	69 (5.98)	5 (2.8)	0.09102 (NS)	74 (5.56)	0	0.40654 (NS)
GDM	81 (7.02)	15 (8.58)	0.4777 (NS)	96 (7.22)	1 (10)	0.8493 (NS)
Preterm labour	104 (9.01)	23 (13.06)	0.08914 (NS)	127 (9.55)	1 (10)	0.92034 (NS)
Abruption	30 (2.6)	3 (1.7)	0.4777 (NS)	33 (2.48)	0	0.5892 (NS)
GDM + hypertensive disorders	15 (1.30)	1 (0.005)	0.40654 (NS)	16 (1.20)	0	0.70394 (NS)
Hypertension disorders						
Gestational hypertension	37 (3.2)	5 (2.84)	0.79486 (NS)	42 (3.16)	1 (10)	0.28914 (NS)
Pre-eclampsia	61 (5.29)	14 (7.95)	0.6818 (NS)	75 (5.64)	1 (10)	0.65272 (NS)
Eclampsia	8 (0.6)	3 (1.7)	0.16758 (NS)	11 (0.08)	0	0.75656 (NS)
History of abortion	211 (18.3)	26 (14.77)	0.25428 (NS)	237 (17.83)	2 (20)	0.78716 (NS)
History of infertility	81 (7.02)	17 (9.65)	0.2113 (NS)	98 (7.37)	0	0.33706 (NS)

Table 4: Fetal outcome.

	Subclinical hypothyroid N (%)	Overt hypothyroid N (%)	P value	Hypothyroid N (%)	Hyperthyroid N (%)	P value
Normal fetus	856 (74.11)	130 (73.86)	0.9442 (NS)	986 (74.07)	9 (81.81)	0.56192 (NS)
Abormal fetus	299 (25.88)	46 (26.13)	0.9442 (NS)	345 (25.92)	2 (18.18)	0.56192 (NS)
Total	1155 (100)	176 (100)	1331	1331 (100)	11 (100)	1342

Table 5: Comparison of fetal abnormality.

Fetal abnormality	Subclinical hypothyroid N (%)	Overt hypothyroid N (%)	P value	Hypothyroid N (%)	Hyperthyroid N (%)	P value
IUGR	98 (8.48)	16 (9.09)	0.78716 (NS)	114 (8.56)	0	0.32218 (NS)
Preterm birth	167 (14.45)	26 (14.77)	0.92828 (NS)	193 (14.50)	2 (18.18%)	0.2113 (NS)
IUD	19 (1.64)	2 (1.13)	0.59612 (NS)	21 (1.57)	0	0.71884 (NS)
IUGR + preterm	11 (0.95)	0	0.18684 (NS)	11 (0.82)	0	0.79486 (NS)
IUD + preterm	4 (0.34)	2 (1.13)	0.14706 (NS)	6 (0.45)	0	0.8493 (NS)
Total	299 (25.88)	46 (26.13)		345 (25.92)	2 (18.18)	

Table 6: comparison of birth weight.

Birth weight	Subclinical hypothyroid N (%)	Overt hypothyroid N (%)	P value	Hypothyroid N (%)	Hyperthyroid N (%)	P value
>2.5 kg	962 (83.29)	150 (85.2)	0.11184 (NS)	1112 (83.54)	8 (72.72)	0.33706 (NS)
2-2.5 kg	170 (14.71)	24 (13.6)	0.70394 (NS)	194 (14.57)	1 (9.09)	0.61006 (NS)
<2 kg	23 (1.99)	2 (11.3)	0.4354 (NS)	25 (18.76)	2 (18.18)	0.00012 (S)
Total	1155 (100)	176 (100)		1331 (100)	11 (100)	

The prevalence of other obstetrical conditions was noted in this cohort and was as such. Preterm prelabour rupture of membranes was present in 5.9% subclinical hypothyroid, 2.7% overt hypothyroid, none of hyperthyroid group. 7% of subclinical hypothyroid women had GDM, 8.5% of overt hypothyroid and 1/10 women in hyperthyroid group had GDM. 9% of women in subclinical hypothyroid group presented in preterm labor, 13% in overt hypothyroid and 1/10 in hyperthyroid group. Abruption was seen in 2.5% of subclinical

hypothyroid women, 1.7% in overt hypothyroid and none in hyperthyroid group. In subclinical hypothyroid group 3.2% women had gestational hypertension, 5.2% had preeclampsia and 0.6% had eclampsia, among the overt hypothyroid, 2.8 had gestational hypertension, 7.9% had preeclampsia and 1.7% had eclampsia. In hyperthyroid group, 1/10 had gestational hypertension, 1/10 had preeclampsia. 18.2% of women in subclinical hypothyroid group had history of abortion, which was present in 14.7% of overt hypothyroid women. 2/10 women in hyperthyroid group had experienced abortion. 7% of women in subclinical hypothyroid group had either a primary or secondary infertility in the past, there were 9.6% of such women in overt hypothyroid group and none among hyperthyroid women. These conditions did not differ significantly among the subclinical and overt hypothyroid and among hyperthyroid and hypothyroid patients, p value was >0.05 (Table 3).

There were 1342 babies born to 1339 mothers (three of the subjects carried twin pregnancy). 25.8% of the babies born were abnormal in terms of less gestational age at birth, low birth weight, IUGR, low apgar and IUD. The fetal outcomes didn't differ significantly between subclinical and overt hypothyroid group and between hyperthyroid and hypothyroid group (Table 4).

On comparing the fetal abnormalities seen in either of the group, the differences again were not of statistical significance (Table 5).

As seen in table 6, there were 222 out of 1342 (16.5%) of babies that had low birth weight <2.5 kg. the difference was not significant in overt hypothyroid and subclinical hypothyroid. But the difference between hypothyroid and hyperthyroid subjects seemed to be statistically significant in terms of birth weight less than 2 kg (p value =0.00012).

Table 7: APGAR score.

Apgar score	Subclinical hypothyroid N (%)	Overt hypothyroid N (%)	P value	Hypothyroid N (%)	Hyperthyroid N (%)	P value
Normal (7-10)	1087 (94.11)	164 (93.18)	0.63122 (NS)	1251 (93.98)	9 (81.81)	0.4009 (NS)
Moderately depressed (4-(	44 (3.8)	8 (4.54)	0.63836 (NS)	52 (3.9)	2 (18.18)	0.50286 (NS)
Severely depressed (1-3)	1 (0.08)	0	0.69654 (NS)	1 (0.07)	0	0.92828 (NS)
IUD fetus (0)	23 (1.99)	4 (2.27)	0.80258 (NS)	27 (20.28)	0	0.63122 (NS)
Total	1155 (100)	176 (100)		1331 (100)	11 (100)	

Table 8: Mode of delivery.

Mode of delivery	Subclinical hypothyroid N (%)	Overt hypothyroid N (%)	P value	Hypothyroid N (%)	Hyperthyroid N (%)	P value
Vaginal	729 (63.2)	104 (59)	0.28914 (NS)	833 (62.6)	6 (60)	0.86502 (NS)
Caesarean	424 (36.8)	72 (41)	0.28914 (NS)	496 (38.4)	4 (40)	0.86502 (NS)
Total	1153	176		1329	10	

The APGAR score at 1 minute of birth was compared in the fetus of our subjects, 54 out of 1342 fetus were moderately depressed (0.03%). There was one fetus severely depressed with apgar score of 2 at 1 minute. The statistical difference wasn't significant between different groups as depicted in Table 7.

Maximum women underwent vaginal delivery, 839 out of 1339 (62.6%). The difference in mode of delivery wasn't significant in the different thyroid disorder groups of women (Table 8).

DISCUSSION

This retrospective cohort study was conducted at department of obstetrics and gynecology at SMGS hospital, Jammu, Jammu and Kashmir, India over a period of 1 year, from January to December 2021. Out of the 15722 women admitted to labour room who had their thyroid profile reports, 89.5% were euthyroid, 10.37% were hypothyroid (8.99% subclinical and 1.37% overt) and 0.06% were hyperthyroid. Among the hypothyroid, 86.7% had subclinical hypothyroidism and 13.3% had overt hypothyroidism. In the study by Dulek et al, 86.7% women were euthyroid, 0.5% were overt hypothyroid, 8.9% were subclinical hypothyroid and 2.8% were hyperthyroid.[3] Gedam et al, in their study reported overt hypothyroidism in 4%, subclinical hypothyroidism in 7.70% women, having overall prevalence of hypothyroidism as 11.70%.[4] Patel et al, found the prevalence of thyroid disorders during pregnancy to be 12.72%, comprising of 9.73% subclinical hypothyroidism, 2.65% overt hypothyroidism and hyperthyroidism in 0.33% women.[5] Murthi et al, observed a prevalence of hypothyroidism of 19.4%.[6]

Prevalence of hypothyroidism has wide geographic variations from 2.5% from the West to 11% from India.[7] Hyperthyroidism on the other hand, is much less common than hypothyroidism, occurring in only 0.5-2/1000 pregnancies.[8]

Thyroid diseases were associated with preterm labour in 104 of 1155 i.e. 9% of subclinical, 23 of 176 i.e. 13% of overt hypothyroidism and 1/10 women in hyperthyroid group. Overall, the prevalence of preterm labour was 9.5% and PPROM was present in 5.5% of women, resulting in 195/1342 (14.5%) preterm births. Patel et al, in their retrospective study found out the prevalence of PPROM to be 3.4% and 11.3% of women gave preterm birth.[5] Likewise, Chaudhary et al, found pprom in 5.2% hypothyroid women and preterm labour in 13.3% hypothyroid women, which were significantly more compared to control.[9]

In this study, 7% of subclinical hypothyroid women had GDM, 8.5% of overt hypothyroid and 1/10 women in hyperthyroid group had GDM. Wahi et al, in their study found the prevalence of GDM to be 6.94% in general population of Jammu region, which was slightly less than our overall prevalence of 7.2% in women with thyroid disorders.[10] Wu et al, on comparing the prevalence of GDM in subclinical hypothyroidism with control group found slightly higher numbers in thyroid disorder than the control, 14.81% versus 11.76% in first trimester and 15.69% versus 12.30% in second trimester.[11]

It was also observed that 10/61 patients of preeclampsia in subclinical hypothyroid group and 1/14 patients of preeclampsia in overt hypothyroidism group had GDM. Making the prevalence of dual endocrinopathy in preeclampsia patients as 14.6%. Gupta et al, found out in their prospective study that 9.75% of preeclampsia patients had dual endocrinopathy.[12] It can be deduced that with such high percentage there will be worsened maternal and fetal prognosis.

Abruption was seen in 2.5% of subclinical hypothyroid women, 1.7% in overt hypothyroid and none in hyperthyroid group. Overall, 2.4% of subjects had abruption. Gandotra et al, carried out a study on outcomes of abruption in the same hospital and they noted that the prevalence of abruption was 2.33% in the general population.[13] Placental abruption was observed more commonly by Breathnach et al, in the setting of either SCH or isolated maternal hypothyroxinaemia when compared with euthyroid controls (p=0.02 and 0.04, respectively) in their study of low risk primigravida women.[14] Similarly, Sharma et al, in their study of prevalence of hypothyroidism in pregnancy and its feto-maternal outcome, came across 8.68% abruption in control group and 21.1% in hypothyroid women.[15]

In subclinical hypothyroid group 3.2% women had gestational hypertension, 5.2% had preeclampsia and 0.6% had eclampsia. Among the overt hypothyroid, 2.8% had gestational hypertension, 7.9% had preeclampsia and 1.7% had eclampsia. In hyperthyroid group, 1/10 had gestational hypertension, 1/10 had preeclampsia. In a retrospective study by Wu et al, subclinical hypothyroidism was associated in 7.4% and 5.4% of patients with hypertensive disorder in first and second trimester respectively, which was significantly more compared to control group.[11] Sharma et al, in their prospective study found the subclinical hypothyroid group to have preeclampsia and eclampsia in 6.6% and 1.3% cases respectively and overt hypothyroid group had 6.6% and 3.4% preeclampsia and eclampsia respectively.[16] Chen et al, compared euthyroid with Subclinical hypothyroidism patient to study maternal outcome and concluded that pregnant women with SCH had increased risk of preeclampsia 3.504%, compared with euthyroid 1.819% with significant p value 0.002.[17]

18.2% of women in subclinical hypothyroid group had history of abortion, which was present in 14.7% of overt hypothyroid women. 2/10 women in hyperthyroid group had experienced abortion. In their study Kalra et al, came across pregnancy loss in their hypothyroid subjects to be 19.7%.[18] Sharma et al, had a bad obstetrical history in 16% of controls and 36.8% of hypothyroid women, which was statistically significant (p=0.04).[15]

7% of women in subclinical hypothyroid group had either a primary or secondary infertility in the past, there were 9.6% of such women in overt hypothyroid group and none among hyperthyroid women. Kumar et al, in their review of effect of hypothyroidism in women found out an association of hypothyroidism with infertility in 22-32% cases.[19] This discrepancy between the review article and our study seems to be present as it is possible that the subjects in our study were only sub fertile and not infertile.

There were 23 IUD in subclinical hypothyroid group and 4 IUD in overt hypothyroid in our study, constituting 2% of pregnancies. Chaudhary et al, also came across increased Incidence if IUD in women with thyroid dysfunction.[9] Subclinical hypothyroid mothers had IUD in 1.4% cases, overt hypothyroid mothers had IUD in 3.2% cases, were significantly more among overt hypothyroidism compared to euthyroid mothers. Pokhanna et al, found out fetal death in 16.6% hypothyroid versus 1.7% control euthyroid women, which was statistically significant (p=0.024).[20]

In this study 3.2% of subclinical hypothyroid and 3.4% of overt hypothyroid mothers carried an IUGR fetus. It was comparable with Chaudhary et al, who had 1.2% and 3.4% IUGR fetus in subclinical and overt hypothyroid group respectively, the control group had only 1.1% IUGR in their study.[9] High incidence of IUGR 9.18% has been reported by Dhara et al, in their study of thyroid disorder in women.[21] Low birth weight <2.5 kg was present in 219/1331 hypothyroid group fetus and 3/11 hyperthyroid group fetus. Overall the incidence of LBW

being 16.5%. Sharma et al, had 40% of fetus of hypothyroid mothers to be LBW. LBW of babies was due to prematurity and IUGR in both of our studies.[16] Sharma et al, had 62.9% LBW fetus in control group and 78.7% LBW in hypothyroid mothers, the difference was statistically significant ($p<0.005$).[15]

APGAR score at 1 minute was normal in 1251/1304 hypothyroid group babies, excluding IUD and 9/11 hyperthyroid group babies. Moderate to severe depression was seen in 53/1304 (4%) hypothyroid and 2/11 (18.1%) hyperthyroid group. Wu et al, observed moderate to severe depression of APGAR in 1.82% of hypothyroid women and 0.62% in control, though the difference wasn't statistically significant ($p=0.07$).[11] In our study 833/1329 (62.6%) delivered vaginally, 496/1329 (38.4%) underwent caesarean section in hypothyroid group and 6/10 (60%) delivered vaginally, 4/10 (40%) underwent caesarean section in hypothyroid group. Sharma et al, similarly had more vaginal (52%) deliveries than caesarean.[16] This was in contrast with Patel et al, where LSCS rates (54.34%) were higher in thyroid disorders because of associated complications like pre-eclampsia, gestational diabetes, IUGR and the difference was statistically significant.[5] High rate of caesarean were also present in study by Dhara et al, where 61% of women with thyroid dysfunction underwent LSCS, maximum patients had LSCS in view of bad obstetrical history.[21]

CONCLUSION

The prevalence of thyroid disorders during pregnancy is significantly more in the present study. Subclinical hypothyroidism was the most common. Adverse maternal and foetal outcomes were almost similar in both subclinical and overt hypothyroidism; hypothyroidism and hyperthyroidism. Monitoring thyroid hormones in women may help to predict and prevent adverse maternal and neonatal outcomes. This immense impact of thyroid disorders warrants routine screening for thyroid dysfunctions in all women in both prenatal and antenatal periods.

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