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Original Research Article

The study of maternal and foetal outcome in pregnant women with thyroid disorder

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ABSTRACT

Background: Thyroid disorder is one of the most common disorder in pregnancy. Thyroid disorder is known to be associated with abnormal maternal and foetal outcomes and overlooked in pregnant women because of non-specific symptoms and hypermetabolic state of pregnancy of pregnancy. It is well established that not only overt, but subclinical thyroid dysfunction also has adverse effects on mother and the foetus like miscarriages, preterm delivery, pre-eclampsia, eclampsia, polyhydramnios, placental abruption, postpartum haemorrhage, low birth weight, neonatal hypothyroidism. Decreased availability of thyroid hormones may also impair neurological and intellectual development of foetus. With this background, we are conducting a study to know the effect of thyroid disorder on pregnancy and its maternal and foetal outcome.

Methods: The present study was conducted in Muzaffarnagar Medical College, Uttar Pradesh, India in collaboration of department of Gynecology and Obstetrics and Pediatrics Department. It is a prospective random cross-sectional study done over 400 pregnant women which includes known cases of thyroid disorder. Serum thyroid stimulating hormone (TSH) test was apart from the routine blood sample investigations as per FOGSI-ICOG good clinical practice recommendation. fT3, fT4 and thyroid peroxidase antibody test were done in patients with a deranged TSH value. Patients were followed up till delivery, and their obstetrics and perinatal outcomes were noted and managed.

Results: In present study out of 400 cases, 25 cases are hypothyroidism and 16 cases are hyperthyroidism in pregnancy. Out of these 41 patients with thyroid dysfunction, complications associated were abortions (14.63%), maternal anaemia (9.7%), pre-eclampsia (12.2%), preterm labour (9.76%), abruption placenta (4.88%), IUGR (2.4%), Still birth (7.32%). Out of 41 patients with thyroid dysfunction, foetal complications seen were hyperbilirubinemia (12.2%), Foetal distress (4.88%), NICU admission (17.07%) and low birth weight (21.95%).

Conclusions: Thyroid disorder in pregnancy have adverse effects on maternal and foetal outcome emphasizing the importance of routine antenatal thyroid screening.

Keywords: Hyperthyroidism, Hypothyroidism, Oligohydramnios, Pregnancy-induced hypertension, Pregnancy, Thyroid dysfunction

INTRODUCTION

Thyroid disorders are encountered frequently during pregnancy and the postpartum period. Thyroid physiology plays a major role in pregnancy, and thyroid disorders constitute one of the most common endocrine disorders in pregnancy. Thyroid diseases are the second

most common endocrine condition encountered in women of childbearing age after diabetes.¹ It has long been recognized that maternal thyroid hormones excess or deficit can influence the outcome for mother and foetus at all stages of pregnancy as well as with ovulation and fertility.² Maternal hypothyroidism is the most common disorder of thyroid function in pregnancy and

has been associated with miscarriage, foetal loss, pre-eclampsia, preterm delivery, placental abruption, low birth weight, foetal distress and reduced intellectual function of the offspring. These adverse outcomes have been associated with overt hypothyroidism found in 0.2% of pregnancies as well as subclinical hypothyroidism found in about 2.3% of pregnancies.³⁻⁶ Subclinical hyperthyroidism is found in 0.4% of pregnancies.⁷ Maternal and foetal complications of hyperthyroidism include congenital heart failure, thyroid storm, hyperemesis gravidarum, pre-eclampsia, preterm delivery, foetal growth restriction, still birth, foetal and neonatal thyrotoxicosis.⁸ Autoimmune thyroid dysfunction remains a common cause of both hyperthyroidism and hypothyroidism in pregnant women.

Graves' disease account for more than 85% of all cases of hyperthyroidism, whereas hashimoto thyroiditis is the most common cause of hypothyroidism.

Postpartum thyroiditis (PPT) reportedly affects 4-10% of women. PPT is an autoimmune thyroid disease that occurs during that first year after delivery. Thyroid dysfunction is often overlooked in pregnant women because of the non-specific and hyper metabolic state of pregnancy.⁹ Hence thyroid function tests become essential to know the thyroid status in pregnancy and also to detect subclinical disease.

METHODS

This is a prospective cross-sectional study conducted on 400 pregnant women attending the Department of Obstetrics and Gynecology, Muzaffarnagar Medical College, Muzaffarnagar Uttar Pradesh over a period of 1 year from January 2018 to December 2018.

All antenatal women in their first trimester, with no other medical disorders, having singleton pregnancy were included in the study.

Patients with known thyroid disorders, multiple gestations and patients with hypertension and diabetes were excluded from the study. After a detailed history and examination, a screening for thyroid disorder was done with serum TSH assay, those with abnormal TSH were subjected to fT4, fT3 and antithyroid peroxidase (TPO) antibody assay.

The reference range used in the study was based on the guidelines of the American thyroid association (ATA) 2017, for the diagnosis and management of thyroid disease during pregnancy and postpartum period. The sample size were 400 patients. The control group includes patients with normal TSH level. The study group includes patients with abnormal TSH levels.

Inclusion criteria

- Age 20-40 years

- Singleton pregnancy
- Gestational age less than 20 weeks.

Exclusion criteria

- Multiple pregnancy
- Known case of thyroid dysfunction controlled on treatment
- Known case of hypertension
- Known case of diabetes
- Known case of heart disease
- Known case of any other medical disorder.

The study tools were predesigned Performa for data collection. TSH reference range: first trimester-0.1-2.5 mIU/L, second trimester- 0.2-3.0 mIU/L, third trimester-0.3-3.0 mIU/L.

Depending on the normal values, patients were classified into

- Subclinical hypothyroidism: High serum TSH with normal fT4 and fT3 levels.
- Overt hypothyroidism: High serum TSH with fT3 and fT4 less than normal.
- Subclinical hyperthyroidism: Low serum TSH with normal fT4 and fT3.
- Overt hyperthyroidism: Low serum TSH with fT3 and fT4 more than normal range.
- Overt hypothyroidism (OH): It is diagnosed with increase in Serum TSH of >10.0 or TSH between 2.5-10.0 with low free T3 and free T4 levels.
- Subclinical hypothyroidism: It is diagnosed with TSH of >2.5 in first trimester and >3.0 in second and third trimester with normal free T3 and free T4 levels.
- Measurement of Anti TPO Ab was done in all hypothyroid patients and a value of >35 were taken abnormal.
- Overt hyperthyroidism: It is diagnosed whenever there is high free T3 and T4 levels with low TSH value less than 0.1.
- Subclinical hyperthyroidism: It is diagnosed when TSH values were low and normal fT3 and fT4 values. Isolated hypothyroxinemia is diagnosed when normal maternal TSH level with free T4 levels in the lower 5th or 10th percentile of reference range is seen.

Women diagnosed with abnormal thyroid functions were referred to endocrinology department for treatment. Hypothyroid patients (both SCH and OH) were treated with levothyroxine and iodine deficiency was corrected. Hyperthyroidism patients were treated with propylthiouracil.

Repeat blood tests were done at 4-6 weeks intervals and dosage of medication were adjusted to keep the serum TSH levels within normal limits.

All the pregnant women enrolled were followed up throughout pregnancy, labour and postpartum period to note any adverse maternal and foetal outcomes.

The maternal outcome was noted in terms of development of abruption, pre-eclampsia, preterm delivery, IUGR, mode of delivery, occurrence of PPH.

Perinatal outcome was noted in terms of low birth weight, still birth, APGAR score at 1minute and 5-minute, neonatal intensive care unit (NICU) admission, neonatal sepsis, neonatal death and development of congenital hypothyroidism.

Statistical analysis

Data was analyzed using statistics package for social science, version 23 SPSS inc Chicago, IL.

Results for continuous variables are presented as mean standard deviation, whereas results for categorical variable are presented as number (percentage). The level $p < 0.05$ was considered as the cut off value for significance.

RESULTS

The present study was done in Muzaffarnagar medical College, Muzaffarnagar, Uttar Pradesh.

A total of 400 patients with thyroid disorder were started on with treatment and s. TSH was repeated every 6-8 weeks and followed up till delivery and outcome were recorded.

A: Demographic distribution of studied patients

Table 1 shows the distribution of patients based on their age and the majority of patients were in the age group 31-35 years (35.25%) followed by 36-40 years age group (24.75%) and the least were of age group below 25 years (16.25%) who had thyroid disorder.

Table 1: Age wise distribution of studied patients.

Age (years)	Frequency n=400	Percentage
≤25	65	16.25
26-30	95	23.75
31-35	141	35.25
36-40	99	24.75

Table 2 to Table 14 distribute the patients based on parity and the majority of patients were primigravida (52.5%) followed by multigravida (47.5%) with thyroid disorder.

Table 3 distributes the studied patients based on their BMI and the majority of patients were having the BMI below 26 kg/m² (43.5%) followed by 26-30 kg/m² (42.0%) while only 14.5% were having >30 kg/m² BMI.

Table 2: Distribution of studied patients on the basis of parity.

Parity	Frequency n=400	Percentage
Primigravida	210	52.5
Multigravida	190	47.5

Table 3: Distribution of studied patients on the basis of BMI.

BMI (kg/m ²)	Frequency n=400	Percentage
≤25	174	43.5
26-30	168	42.0
>30	58	14.5

Table 4 depicts the residence location of the studied patients and the majority of patients were from rural area (73%) followed by urban location (27%).

Table 4: Distribution of studied patients on the basis of residence.

Residence	Frequency n=400	Percentage
Rural	292	73
Urban	108	27

Table 5 shows the socio-economic status of the studied patients and the majority of patients were from middle class (41.75%) followed by lower middle class (35.75%) and the least were of upper-class status (3.50%).

The pattern of thyroid dysfunction among antenatal women and correlation with demographic parameters.

Table 5: Distribution of studied patients on the basis of socio-economic status.

Socio-economic status	Frequency n=400	Percentage
Lower	27	06.75
Lower middle	143	35.75
Middle	167	41.75
Upper middle	49	12.25
Upper	14	03.50

B: The pattern of thyroid dysfunction among antenatal women and correlation with demographic parameter

Table 6 distributes the patients having hypothyroidism with 22 subclinical and 3 overt while hyperthyroidism was found in 16 patients with subclinical in 13 and overt in 3.

Table 7 shows the distribution of normal and thyroid dysfunction patients based on age and the association is found to be statistically insignificant ($P > 0.05$). Table 8 shows the distribution of normal and thyroid dysfunction

patients based on parity and the association is found to be statistically insignificant ($P>0.05$).

Table 6: Distribution of studied patients on the basis of thyroid disorder.

Thyroid disorder	Frequency n=400	Percentage
Normal	359	89.75
Hypo-thyroidism	Subclinical	22
	Overt	3
Hyper-thyroidism	Subclinical	13
	Overt	3

Table 7: Age wise distribution of normal and thyroid dysfunction patients.

Age (years)	Normal n=359	Thyroid dysfunction n=41	P value
<25	58 (16.16%)	7 (17.07%)	0.991
26-30	86 (23.98%)	9 (21.95%)	
31-35	126 (35.10%)	15 (36.59%)	
36-40	89 (24.79%)	10 (24.39%)	

*Chi square test/fishers test

Table 8: Distribution of normal and thyroid dysfunction patients on the basis of parity.

Parity	Normal (n=359)	Thyroid dysfunction (n=41)	P value
Single	188 (52.37%)	22 (53.66%)	0.874
Multiple	171 (47.63%)	19 (46.34%)	

*Chi square test/fishers test

Table 9: Distribution of normal and thyroid dysfunction patients on the basis of BMI.

BMI (kg/m ²)	Normal n=359	Thyroid dysfunction n=41	P value
<25	172 (47.91%)	2 (4.88%)	<0.001
26-30	158 (44.01%)	10 (24.39%)	
≥30	29 (8.08%)	29 (70.73%)	

Table 9 shows the distribution of normal and thyroid dysfunction patients based on BMI and the association is found to be statistically significant ($p<0.05$).

Table 10 shows the distribution of normal and thyroid dysfunction patients based on residence and the association is found to be statistically insignificant ($P>0.05$).

Table 10: Residence wise distribution of normal and thyroid dysfunction patients.

Residence	Normal n=359	Thyroid dysfunction n=41	P-value
Rural	263 (73.26%)	29 (70.73%)	0.730
Urban	96 (26.74%)	12 (29.27%)	

*Chi square test/fishers test

Table 11: Socio-economic status wise distribution of normal and thyroid dysfunction patients.

Socio-economic status	Normal n=359 (%)	Thyroid dysfunction n=41 (%)	P-value
Lower	24 (6.69)	3 (7.32)	0.367
Lower middle	133 (37.05)	10 (24.39)	
Middle	144 (40.11)	23 (56.10)	
Upper middle	45 (12.53)	4 (9.76)	
Upper	13 (3.62)	1 (2.44)	

Table 11 shows the distribution of normal and thyroid dysfunction patients based on Socio-Economic Status and the association is found to be statistically insignificant ($p>0.05$).

Table 12 shows the maternal complications in different thyroid dysfunction and majority of patients were of abortion (31) followed by maternal anaemia and IUGR with 24 each, preterm delivery (22) and the least complications were of abruption placentae (2) and pre-eclampsia (5).

Table 12: Maternal complications in different thyroid dysfunction patients.

Maternal complications	Normal	Hypothyroidism		Hyperthyroidism		Total n=400
	Mean	Subclinical	Overt	Subclinical	Overt	
Abortion	25	2	0	2	2	31
Maternal anaemia	20	4	0	0	0	24
Pre-eclampsia	0	4	0	1	0	5
Preterm delivery	18	0	1	3	0	22
Still birth	8	1	1	1	0	11
IUGR	23	1	0	0	0	24
Abruptio placentae	0	1	0	1	0	2
Total	94/359	13/22	2/3	8/13	2/3	119/400

Table 13: Maternal complications in different thyroid dysfunction patients.

Complications	Normal n=359	Thyroid dysfunction n=41	P value
Abortion	25 (6.69%)	6 (14.63%)	0.082
Maternal anaemia	20 (5.57%)	4 (9.76%)	0.285
Pre-eclampsia	0 (0.0%)	5 (12.20%)	<0.001
Preterm delivery	18 (5.01%)	4 (9.76%)	0.207
Still birth	8 (2.23%)	3 (7.32%)	0.059
IUGR	23 (6.41%)	1 (2.44%)	0.312
Abruptio placentae	0 (0.0%)	2 (4.88%)	<0.001
Total	94/359	25/41	<0.001

*Chi square/fishers test

Table 14: Correlation between normal and thyroid dysfunction in term of foetal complication.

Foetal complications	Normal n=359	Thyroid dysfunction n=41	P value
Low birth weight	24 (6.69%)	9 (21.95%)	<0.001
Hyperbilirubinemia	11 (3.06%)	5 (12.20%)	0.004
Foetal distress	17 (4.74%)	2 (4.88%)	0.120
NICU admission	26 (7.24%)	7 (17.07%)	0.030
Total	78/359	23/41	<0.001

Tables 12 to 14 shows the correlation between normal and thyroid dysfunction in term of maternal complication and the association was found to be statistically significant ($p < 0.05$) in cases of pre-eclampsia and abruption placenta while rest of the complications have shown insignificant association ($p > 0.05$). Table 13 shows the correlation between normal and thyroid dysfunction in term of foetal complications where foetal distress was having insignificant association ($P \geq 0.05$) while other complications like low birth weight, hyperbilirubinemia and NICU admissions were having statistically significant association ($p < 0.05$).

DISCUSSION

Thyroid disorder is one of the most common endocrine disorder in women during pregnancy and is associated with adverse maternal and foetal outcomes in pregnancy. However, an early detection of thyroid dysfunction and treatment of mother during gestation improves the outcome. Early detection of thyroid during pregnancy is possible if the patient is advised thyroid function test during her first perinatal visit soon after the pregnancy is confirmed. The most frequent thyroid disorder in pregnancy is maternal hypothyroidism. There is a geographic variation in prevalence of hypothyroidism during pregnancy. It varies from 2.5% in the west to up to 11% in India.¹⁰ Prevalence of hypothyroidism was found to be more in Asian countries compared with that in the western countries. Untreated or inadequately treated and subclinical hypothyroidism all are associated with increased risk of miscarriage, pre-eclampsia, anaemia, foetal growth restriction, placental abruption, perinatal and neonatal morbidity and mortality, preterm delivery, small head circumference, low birth weight and impaired

neuropsychological development.¹¹ The prevalence of hyperthyroidism during pregnancy is less common (0.6%) than hypothyroidism.¹² 10-20% of euthyroid pregnant women are positive for anti TPO antibodies or anti thyroglobulin antibodies in the first trimester and significant number of them will develop Hypothyroidism ($TSH > 3 \text{ mIU/l}$) in third trimester and postpartum thyroiditis.¹³ In present study the mean age was observed as 31.58 ± 5.08 years (Table 1) and similar results were obtained in various past studies e.g. Abdulslam K et al, and Irinyenikan et al, have observed the mean age of the studied patient as 27.70 ± 7.80 years and 30.40 ± 4.62 years respectively.^{14,15} This implies that 3rd decade of life is the ideal age for pregnancy among the patient with gestational hyperthyroidism or hypothyroidism.

In present study the prevalence of thyroid dysfunction out of 400 studied patients was found to be 10.25% and comparable results were observed by Mulik J et al, in where the prevalence of thyroid dysfunction was 12.15%.¹⁶

In present study the prevalence of subclinical hypothyroidism was found to be 5.50% and overt hypothyroidism as 0.75% while hyperthyroidism was observed as 3.25% to be subclinical and 0.75% to be overt (Table 6).

This means that hypothyroidism, that too Subclinical Hypothyroidism is more common in pregnant women than hyperthyroidism. Studies done by Gayathri R et al, and Nazarpour S et al, also reported hypothyroidism as more common than hyperthyroidism.^{17,18} Association

between normal and thyroid dysfunction patients with respect to age.

In present study the association between normal and thyroid dysfunction patient with respect to age was found to be statistically insignificant ($p>0.05$) with majority of patient in the age group ranging from 31-35years (Table 7). Similar association was also observed by Ezzeddine D et al, and stated that age do not play a significant role in patients with thyroid dysfunction ($p>0.05$).¹⁹ The studies done by Vaidhya B et al, showed a lower age compared to the western studies.²⁰ This is due to the early marriage and conception prevalent in our area. There is a paucity of studies analyzing the association of age with hypothyroidism in pregnancy, probably due to the physiological changes in thyroid function during pregnancy. The guidelines of American thyroid association from 2011 included age over 30 years as one of the risk factors for hypothyroidism in pregnancy.

Normal and thyroid dysfunction patient on the basis of parity. In present study the association of parity with normal pregnant women and the women suffering from thyroid dysfunction shows statistically insignificant association i.e. $p>0.05$ (Table 8). Ezzeddine D et al, in their study in 2017 reported the similar results as in present study ($p>0.05$) and Prasad DR et al, also reported that the association between parity and hypothyroidism has no statistical significance with respect to parity ($p>0.05$).^{19,21}

A study by Nirmal CV et al, about national outcome of hypothyroidism in pregnancy- a south Indian study also showed no statistical difference with respect to parity in different groups.²² This implies parity do not play any significant role for the prevalence of thyroid function.

Normal and thyroid dysfunction patients on the basis of BMI. In our study we observed a statistically significant association ($p<0.05$) of BMI with normal and the women suffering from thyroid dysfunction (Table 9). Pillai NS et al, also reported an increased risk of thyroid dysfunction in pregnancy with the increase in BMI($p=0.015$) in their study in 2018.²³ This shows that BMI play a significant role in the prevalence of thyroid dysfunction, as the BMI increases prevalence of thyroid dysfunction also increases significantly.

Normal and thyroid dysfunction patients on the basis of residence (urban and rural). In the present study we observed that the association between region with thyroid dysfunction was found to be statistically insignificant ($p>0.05$) (Table 10). Gupta HP et al, also reported that no association of region was observed with thyroid disorder($p<0.05$) in their study in 2015.²⁴ Normal and thyroid dysfunction patients on the basis of Socio-economic status.

In the present study majority of women were from the middle socio-economic status (41.75%) (Table 5) and

there was statistically insignificant association ($p>0.05$) between socio-economic status and thyroid disorders in pregnant women (Table 11). Manju VK et al, reported the similar results as in present in present study.²⁵ Maternal complications in thyroid dysfunction and correlation between them in the present study the maternal complications in different thyroid dysfunction and majority of patients were of abortion (31 patients) followed by maternal anaemia and IUGR (24 patients each). 22 cases were of preterm delivery and the least complications were of abruptio placenta and pre-eclampsia (Table 12). The association was found to be statistically significant ($p<0.05$) in pre-eclampsia and abruptio placenta (Table 13) with $p<0.001$. Manju VK et al, and Sathiamma PK et al, also reported the similar complications in their respective studies.²⁵ Gupta HP et al, also reported significant association ($p<0.05$) in pre-eclampsia and abruptio placentae.²⁴ Thyroid disorder has a significant influence over metabolic and physiological activities and hence these eventually affect the maternal and foetal well-being. Normal and thyroid dysfunction in term of foetal complication and correlation between them. In the present study the correlation between normal and thyroid dysfunction in term of foetal complication was that, foetal distress was having insignificant association ($p>0.05$) while other complications like low birth weight, hyperbilirubinemia and NICU admission were having statistically significant association ($p<0.05$) (Table 14). Gupta HP et al, reported thyroid disorders have a significant ($p<0.05$) influence over metabolic and physiological activities and hence these eventually affects the maternal and foetal well-being.²⁴ Prasad DR et al, reported 21.4% babies with neonatal hyperbilirubinemia were born to hypothyroid women compared to 16.5% babies born to euthyroid women.²¹ This is statistically insignificant ($p>0.05$). Similar to present study, Ajmani SN et al, observed that the incidence of neonatal hyperbilirubinemia in normal population was 6.1% in subclinical hypothyroidism and 11.8% in overt hypothyroidism with statistical significance ($p<0.05$).²⁶ Dhanwal DK et al, also reported significant ($p<0.05$) adverse effects on maternal and foetal outcome emphasizing the importance of routine antenatal thyroid screening.²⁷ Therefore, findings of our study are consistent with other previous reported data from India and this study also shows a rising trend of hypothyroidism among the Indian pregnant women.

Limitations of this study was a descriptive cross-sectional study where the investigators had only one encounter with the study participants. Some of the participants that were found to be normotensive and euthyroid during the course of study might have become hypertensive or developed some forms of thyroid dysfunction afterwards.

Recommendations

Pre-eclampsia clinics should be introduced in our hospitals aimed at screening women planning to conceive. Some of the biochemical investigations that

may be performed include fasting blood glucose, total cholesterol, low density lipoprotein cholesterol, triglycerides. All pregnant women should be encouraged to enroll for antenatal care at an early gestational age. This will ensure early screening for medical disorders such as hypertension, diabetes and various forms of thyroid dysfunction. Reference intervals for all thyroid function test parameters should be developed. These should include those for pregnant women generally and trimester specific reference interval in particular. Further studies are required to evaluate impact of thyroid disorder during pregnancy in the Indian population to decide whether universal screening is needed for Indian pregnant women.

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