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Original Research Article

Thyroid Disorders in Pregnancy and Pregnancy Outcomes

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Abstract

Thyroid disorders constitute one of the most common endocrine disorders seen in pregnancy. Thyroid disorder in pregnancy is associated with adverse obstetrical and fetal outcomes.

Material and Methods*:* The present study was prospective observational study conducted in tertiary medical hospital in Mumbai. Study was conducted over duration of 6 months. 85 patients fulfilled inclusion criteria and were enrolled in study. Patients were diagnosed as overt hypothyroid or subclinical hypothyroid. TPO antibody was done in hypothyroid patients. Patients were treated with thyroxine as per protocol.

Result: Most of pregnant patients with thyroid dysfunctions were in age group of 20-30 years (75%). 52.9% had gestational age between 24-36 weeks. Subclinical thyroid disease was present in 94.1% while overt thyroid disease was seen in 5.9% of patients. Sub clinical and overt hypothyroidism was common in gestational age group of 24-36 weeks. Thyroperoxidase antibodies tested positive in 70.6% patients. Subclinical hypothyroidism 80% patients underwent normal delivery while 12% patients had abortion. In patients having overt hypothyroidism, 2 patients underwent normal delivery while 3 patients had abortion.

Conclusion: Early detection of thyroid disorders in pregnancy leads to safe pregnancy with minimal maternal and fetal complication. Subclinical hypothyroidism is the commonest thyroid dysfunction in pregnancy.

Keywords: thyroid dysfunction, pregnancy, hypothyroid, Thyroperoxidase antibodies, thyroxine

Introduction

Thyroid disorders constitute one of the most common endocrine disorder seen in pregnancy. It is the second most common endocrine condition in pregnant women after diabetes. The production of thyroid hormone and iodine requirement increases by 50% during pregnancy. Pregnancy is the stress test for thyroid gland. Women with iodine deficiency, autoimmunity and limited thyroid reserve develop hypothyroidism during

pregnancy. Thyroid disorder in pregnancy is associated with adverse obstetrical and fetal outcomes. Obstetrical complications like abortion, pre-eclampsia, abruptio placenta, preterm labor, post-partum hemorrhage can occur in thyroid dysfunction in pregnancy, while fetal complication like prematurity, low birth weight, still birth, perinatal death, IUGR and neonatal thyroid disorder can occur in thyroid dysfunction in pregnancy. There is paucity of data on prevalence of thyroid dysfunction in Indian pregnant women. Prevalence range from 4.8 to 11% [1,2]. Some studies estimate prevalence of maternal hypothyroidism to be 10-13% and that of maternal hyperthyroidism to be 0.4 - 1.7% [3]. Western literature show prevalence of hypothyroidism in pregnancy to be 2.5 % [4] and that of hyperthyroidism in pregnancy to be 0.1-0.4 % [5].

Following physiological and hormonal changes occur in pregnancy as there is increase in thyroid requirement in pregnancy a) There is increased thyroxine production by 50%, b) Increased iodine requirement by 50% due to increased iodine utilization, increased iodine renal clearance and increased thyroglobulin production c) Increase thyroid hormone metabolism as pregnancy is hypermetabolic state, d) Increased thyroxine binding globulin (TBG) level by 2 fold due to increased estrogen levels in pregnancy which increases TBG production and decreases TBG clearance [6], e) Increased total T4 and total T3 due to increase TBG (total T4 increases 1.5 fold higher than non-pregnant state by 16 weeks of gestation), f) Decreased TSH in 1st trimester occurs due to HCG stimulation of TSH receptor thereby increasing T4 production [7,8]. HCG stimulates TSH by having common alpha subunit and unique beta subunit. HCG level in pregnancy peaks at 10-12 weeks resulting in transient physiological subclinical hyperthyroidism in 1st trimester, which should be monitored and does not require treatment. WHO recommended 250 mcg of iodine intake daily in pregnancy and lactation while ATA recommended 150 mcg of iodine intake daily. Fetal thyroid gland become functional in 2nd trimester. Fetus is dependent on maternal thyroxine in 1st trimester for growth and development. Maternal hypothyroidism in 1st trimester can be harmful to the fetal brain development and can lead to poor cognitive and scholastic performance in childhood. Commonest cause of hypothyroidism in pregnancy is low iodine intake followed by chronic autoimmune thyroiditis.

The objective of the study was to evaluate thyroid dysfunction in pregnancy and to study multiple parameters including age of presentation, gravida, gestational age, presence of TPO antibodies, treatment of thyroid disease and outcome.

Material and Methods

The present study was prospective observational study conducted in tertiary medical hospital in Mumbai. Ethics committee permission was obtained before commencement of study. Study was conducted over duration of 6 months from June 2019 to December 2019 and subject were recruited from medicine OPD and endocrine OPD after obtaining due consent.

Total number of 560 patients were screened for thyroid disease and 85 patients fulfilled inclusion criteria and were enrolled in study. All pregnant patients having thyroid disorder were included in study. Pregnant patients having central hypothyroidism, renal, hepatic involvement were excluded from study. Details of patients were recorded in case record forms. Detailed history included symptoms of thyroid illness, past medical history, history of chronic medicine intake, demographic data and past obstetric history. Obstetric history included gravida, parity, and history of miscarriage, preterm delivery or any other complication in past pregnancy. Vital parameters, local examination of

thyroid, general examination and systemic examination was done and noted in case record form. Each patient was screened for risk factors. Personal and family history of thyroid dysfunction was recorded. Each patient underwent following investigation like complete blood count, bleeding time, clotting time, blood sugar, renal function test, liver function test, blood group and cross matching, HIV ELISA and urine routine microscopy.

Gestational age of pregnancy was calculated from last menstrual period and verified by ultrasonography. Pregnancy was confirmed clinically and by ultrasonography.

Patients having goitre underwent USG neck. Thyroiditis was considered if thyroid ultrasonography showed the following findings: a) increased vascularity, normal or decreased flow on color Doppler, b) Diffused enlarged thyroid gland with heterogeneous echotexture, c) Hypoechoic micro nodules (1-6 mm) with surrounding echogenic septate (Giraffe pattern).

After overnight fasting for 12 – 14 hours, 5ml blood was collected for thyroid function test. TSH, FT3, FT4 were measured using electro-chemiluminesence immunoassay (Roche Elecsys band Switzerland). TPO antibodies was done in patients found to be hypothyroid (overt or subclinical).

Patients were diagnosed as a) Overt hypothyroid if TSH was high with low FT4 level, b) Subclinical hypothyroid if TSH was high with normal FT4 level. Both patients were treated with thyroxine at dose of 1.6 mcg/kg and 1 mcg/kg/day respectively. Also patients with TSH 2.5 to 4 mIU/L with TPO antibody positivity were treated with thyroxine at dose of 1mcg/kg/day. For patients with pre-pregnancy hypothyroidism on thyroxine, there thyroxine doses were increased by 30% of baseline dose and were monitored as per protocol.

Tablet thyroxine was taken on empty stomach in morning, 45 minutes before breakfast. Calcium, iron and vitamin supplements were avoided within 4 hours of intake of thyroxine tablet as they decrease thyroxine absorption in intestine.

Our goal was to keep TSH in trimester specific range and FT4 in upper normal range [9]. The reference ranges of TSH, FT3, FT4 were as per guideline of American Thyroid Associations (ATA) for diagnosis and management of thyroid disease during pregnancy and postpartum. The normal reference range for TSH were following as per recommendation of ATA [10]i) First trimester 0.1 – 2.5 mIU/L ii) Second trimester 0.2 – 3.0 mIU/L, iii) Third trimester 0.3 – 3.0 mIU/L. Normal FT4 range 0.7 – 1.8 ng/ml. Normal FT3 range 1.7 – 4.2 pg/ml.

TSH, FT3, FT4 were done four weekly in first trimester, once in second trimester and once in third trimester. Patients were followed till full term and outcomes recorded. Patients having TPO antibody with hypothyroidism were labeled as Hashimoto thyroiditis. Postpartum patients with gestational subclinical hypothyroidism were advised to stop thyroxine treatment. Those patients with overt hypothyroidism in gestation had their thyroxine dose decreased by 50% in postpartum period. Those who had pre-pregnancy hypothyroidism and were on thyroxine treatment in pre-pregnant peroid, their thyroxine dose was decreased by 50% or converted to prepregnant thyroxine dose in postpartum period. Patients were monitored for development of post-partum thyroiditis. Thyroid function test was repeated 6 weeks postpartum.

Statistical analysis were done using open epi software version 2.3.1 and SPSS software 21. All data was compiled in excel and qualitative data was depicted using percentage and quantitative data by mean. Appropriate test of analysis i.e chi square test and t test was applied.

Result

This study which was prospective observational study of thyroid dysfunction in pregnancy. Total 560 pregnant patients were screened for thyroid dysfunction out of which 85 pregnant patients were enrolled in the study. Patients coming to medicine OPD and endocrine OPD in our tertiary care hospital were recruited for the study.

Most of pregnant patients with thyroid dysfunctions were in age group of 20-30 years (75%) followed by age group 30-40 years (17.6%) and less than 20 years (7.05%) (Table 1). 52.9% pregnant patients with thyroid dysfunctions had gestational age 24-36 weeks followed by 44.7% patients in gestational age 12-24 weeks and 2.4% patients in gestational age 0-12 weeks (table 1). Out of 85 pregnant patients included in study, 3.5% patients had previous history of thyroid illness while 96.4% patients did not give past history of thyroid illness (table 1).

In this study, 9.4 % of pregnant patients had history of abortion while 90.6% patients did not have history of abortion (table 1). Subclinical thyroid disease was present in 94.1% pregnant patients while overt thyroid disease was seen in 5.9% of patients (table 1). In study group, 7% of the patients had diabetes. Thyroperoxidase antibodies tested positive in 70.6% patients while 29.4% of patients had tested negative for thyroperoxidase antibodies (table 1). 61.1% patients had thyroiditis on sonography while 38.9% patients had normal thyroid on sonography (table 1). Patients having subclinical and overt hypothyroidism were treated with thyroxine tablet which was given in morning one hour before breakfast. In this study, 54.1% of patients were treated with tablet thyroxine 25 mcg, while 10.5% of the patients were treated with tablet thyroxine 75 mcg. 5.9% of patients required tablet thyroxine 100mcg while 1% of patient required tablet thyroxine 125 mcg and above. Out of 85 patients included in this study, 45.8% patients were gravida two, 41.2% patients were gravida one, 11.7% patients were gravida 3 and 1 % patient were gravida 4 (table 1).

In this study group, 56 patients with subclinical thyroid disease tested positive for thyroperoxidase antibody while 4 patients having overt thyroid disease tested positive for thyroperoxidase antibodies (table 2). Sub clinical thyroid disease was common in gestational age group 24-36 weeks (42 patients) and 12-24 weeks (37 patients) while overt thyroid disease was common in gestational age group of 24-36 weeks (3 patients)(table 3). Out of 80 patients with subclinical hypothyroidism 71(80%) patients underwent normal delivery while 9 (12%) patients had abortion. Out of 5 patients with overt hypothyroidism 2 patients underwent normal delivery while 3 patients had abortion suggestive poor delivery outcome in patients having overt hypothyroidism (P=0.001, significant) (table 4).

Table 1: Demographic and Investigations

Parameters		Numbers	Percentage
Age	Less than 20	6	7.05
	20-30	64	75.2
	30-40	15	17.6
	More than 40	0	0
Gestational age (weeks)	0-12	2	2.3
	12-24	38	44.7
	24-36	45	52.9
Gravida	G1	35	41.2

	G2	39	45.8
	G3	10	11.7
	G4	1	1.1
History of thyroid disease	Yes	8	9.4
	No	77	90.6
History of abortion	Yes	8	9.4
	No	77	90.6
Thyroid disease	Overt hypothyroidism	5	5.9
	Subclinical hypothyroidism	80	94.1
TPO positivity	Yes	60	70.6
	No	25	29.4
USG thyroid	Thyroiditis	52	61.1
	No abnormality	33	38.9

Table 2: Association between thyroid disease and TPO antibodies

Thyroid Disease	**TPO**		**Total**
	Yes	**No**	
Overt hypothyroidism	4	1	5
Subclinical hypothyroidism	56	24	80
Total	60	25	85

Applying Chi square test, p= 0.31. As p value is >0.05 it shows no statistical significance

Table 3: Association between thyroid disease and gestational age

Thyroid disease	**Gestational age (weeks)**			**Total**
	0-12	**12-24**	**24-36**	
Overt hypothyroidism	1	1	3	5
Subclinical hypothyroidism	1	37	42	80
Total	2	38	45	85

Applying Chi square test, p= 0.02. As p value is < 0.05 it shows statistical significance

Table 4: Association between thyroid disease and outcome

Thyroid Disease	**Outcome**		**Total**
	Normal delivery	**Abortion**	
Overt hypothyroidism	2	3	5
Subclinical hypothyroidism	71	9	80
Total	73	12	85

Applying Chi square test, p= 0.001. As p value is <0.05 it shows statistical significance

Discussion

In this study the prevalence of hypothyroidism in pregnancy was 15%. Mahadik k *et al* and Ramchandra R *et al* in there study found prevalence of thyroid disorder in pregnancy to be 11% and 22.39% respectively [11-12]. While kalawati *et al*, pahwa *et al*, and Ramchandra *et al* found prevalence of 6.5%, 10% and 22.39% respectively [12-14]. Most of pregnant patients with thyroid dysfunction were in age group 20-30 years (75%) followed by age group 30-40 years (17.6%) and age group less than 20 years (7.05%). Kalawati *et al* in their study found 72.5% patients were in age

group 20-25 years [13]. Pahwa S *et al* found prevalence of thyroid disease of 20.6% in age group of 21-25 years and 2.9% in pregnant women of age less than 21 years [14].

In this study 94.1% pregnant patients had subclinical hypothyroidism and 5.9% pregnant patients had overt hypothyroidism (p=0.02). Pahwa S *et al* in their study found 6% pregnant patient had subclinical hypothyroidism, 2% had overt hypothyroidism and 2% had subclinical hyperthyroidism [14] while Mahadik K *et al* found 5.6% pregnant patient had subclinical hypothyroidism, 3.5% had overt hypothyroidism and 1.5% had subclinical hyperthyroidism [11]. Ramchandran R *et al* found 20.63% pregnant patient had subclinical hypothyroidism [12].

In this study 52.9% pregnant patients had gestational age 24-36 weeks, 44.7% had gestational age 12-24 weeks while 2.4% patients had gestational age 0-12 weeks suggestive of late detection of thyroid dysfunction by 3rd trimester. This stresses the importance of early screening for thyroid dysfunction which should be mandatory in all pregnant patients in India. This will prevent not only the pregnancy complication related to thyroid dysfunction but also avoid cognition related issue in offspring in future. Kalawati *et al* in their study found two third of patients in gestational age group 8-12 weeks [13].

Thyroperoxidase antibody was present in 70.6% patients while 29.4% patients did not have TPO antibody. Out of 60 patients who had TPO antibodies, 56 patients had subclinical hypothyroidism and 4 patients had overt hypothyroidism. Ramchandra R *et al* found 9.9% pregnant patients had TPO antibody [12]. The prevalence of TPO antibody in euthyroid pregnant patients has been shown to be associated with increased number of miscarriage, peri natal death and low motor and intellectual development in offspring [15]. But the role of thyroxine treatment in euthyroid pregnant patients having TPO antibody is debatable.

Out of 80 pregnant patient with subclinical hypothyroidism 88% underwent normal delivery while 12% patients had abortion. Out of 5 pregnant patient with overt hypothyroidism, 2 patients underwent normal delivery while 3 patients had abortions suggestive of poor outcome in patients with overt hypothyroidism (p=0.001). Ramchandra R *et al* in her study found 8.2% patients had spontaneous miscarriage [12]. A good outcome of deliveries in our study attributed to early onset of treatment with tablet thyroxine in hypothyroid pregnant patients , which again stresses the importance of universal screening, early detection of thyroid disease in initial stages followed by appropriate treatment.

Out of 85 patients included in study 3.5% patients had previous history of thyroid illness while 96.4% patients did not give past history of thyroid illness denoting urgent need for thyroid disease surveillance in pregnant population. Those patients who had past history of thyroid illness and were on thyroxine treatment, their thyroid doses were increased by 30% so that trimester specific TSH and FT4 goal were achieved.

9.4% of pregnant patients gave history of abortion in previous pregnancy these patients were meticulously monitored for development of overt or subclinical hypothyroidism by doing thyroid function test at recommended intervals. 54% of pregnant hypothyroid patients required low dose of thyroxine which suggests that good outcomes and target TSH goals can be achieved with minimal dose of thyroxine with regular monitoring.

61% of pregnant hypothyroid patients had thyroiditis on USG while 70% patients had TPO antibodies denoting sonological finding of thyroiditis was indirect markers of TPO antibody positivity and Hashimotos thyroiditis.

Limitations of study were a) need to study large pregnant population in urban and rural regions, b) long term follow up of patients in post-partum period for their thyroid disorder.

Conclusion

Early detection of thyroid disorders in pregnancy by thyroid function test followed by effective, aggressive treatment leads to safe pregnancy with minimal maternal and fetal complications. This study showed that subclinical hypothyroidism is the commonest thyroid dysfunction in pregnancy and there is high prevalence of TPO antibodies in pregnant patients with thyroid dysfunction.

References

1. Nambiar V, Jagtap VS, Sarathi V, Lila AR, Kamalanathan S, Bandgar TR *et al*. Prevalence and impact of thyroid disorders on maternal outcome in Asian Indian pregnant women. J Thyroid Res., 2011; 2011: 4290- 4297.
2. Sahu MT, Das V, Mittal S, Agarwal A, Sahu M. Overt and subclinical thyroid dysfunction among Indian pregnant women and its effect on maternal and fetal outcome. Archives of Gynecology and Obstetrics, 2010; 281(2): 215–220.
3. Dhanwal DK, Bajaj S, Rajput R, Subramaniam KA, Chowdhury S, Bhandari R, *et al*. Prevalence of hypothyroidism in pregnancy: An epidemiological study from 11 cities in 9 states of India. Indian J Endocrinol Metab 2016; 20:387-90.
4. LeBeau SO, Mandel SJ. Thyroid disorders during pregnancy. Endocrinology Metabolism Clinics of North America. 2006; 35(1): 117-136.
5. Hollowell JG, Staehling NW, Flanders WD, Hannon WH, Gunter EW, Spencer CA *et al*. Serum TSH, T4, and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). Journal of Clinical Endocrinology and Metabolism. 2002; 87(2): 489-499.
6. Ain KB, Mori Y, Refetoff S. Reduced clearance rate of thyroxine-binding globulin (TBG) with increased sialylation: a mechanism for estrogen-induced elevation of serum TBG concentration. J Clin Endocrinol Metab1987; 65:689.
7. Williams GR. Neurodevelopmental and neurophysiological actions of thyroid hormone. J Neuroendocrinol. 2008; 20: 784–94.
8. Glinoer D. The regulation of thyroid function in pregnancy: Pathways of endocrine adaptation from physiology to pathology. Endocr Rev. 1997; 18:404–33.
9. Bhattacharyya A, Wright JD, Vice PA. Obstetric difficulties due to Graves' disease. Postgrad Med J. 2002; 77: 661: 669-70.
10. Stagnaro-Green A, Abalovich M, Alexander E, Azizi F, Mestman J, Negro R *et al*. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. Thyroid. 2011; 21:1081–125.
11. Mahadik K., Choudhary P., Roy P. K. Study of thyroid function in pregnancy, it's feto-maternal outcome; a prospective observational study. BMC pregnancy and childbirth. 2020; 20:769.
12. Ramchandran R., Mohan L., Jose M.S. Prevalence of thyroid disorder in antenatal women and it's impact on maternal and foetal outcome. Indian journal of forensic and community medicine January- March; 2020;7(1):29-32.
13. Biradar K.D. Hypothyroidism in pregnancy: A Hospital based cross sectional study. Indian Journal of obstetrics and Gynecology Research 2016; 3(2): 137- 139.
14. Pahwa S, Mangat S. Prevalence of thyroid disorder in pregnancy.

International Journal of Reproduction, contraception, obstetrics and Gynecology.2012 Sep 7(9):3493-3496.
15. Matalon ST, Blank M, Ornoy A, Shoenfeld Y. The association between anti-thyroid antibodies and pregnancy loss. Am J Reprod Immunol. 2001; 45:72–7.