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Assessment of Thyroid Disorder in Pregnancy and Its Effect on Pregnancy Outcome in a Tertiary Healthcare Institute in Soutehrn Maharashtra: A Prospective Study

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Abstract

Context: Thyroid disorders are the second most common endocrinology disorder found in pregnancy. Women with thyroid dysfunction both overt and subclinical are at increased risk of pregnancy-related complications such as threatened abortion, preeclampsia, preterm labor, placental abruption, and postpartum hemorrhage. *Materials and Methods:* The present prospective analytical study was conducted among pregnant women to assess the prevalence of thyroid disorders among them and to observe the obstetric outcomes of these women suffering from thyroid disorders during the period of two years. *Results:* In the present study, 62 out of 1000 pregnant women screened had thyroid disorders. The prevalence of thyroid disorders in our study was 6.2%. The prevalence of subclinical hypothyroidism, overt hypothyroidism, subclinical hyperthyroidism and hyperthyroidism was 3.6%, 1.6%, 0.8% and 0.2% respectively. *Conclusions:* Thyroid dysfunction is a condition that should be treated aggressively and affects a significant number of women during pregnancy associated with adverse maternal outcome.

Keywords: Thyroid Disorders in Pregnancy; Hypothyroidism; Hyperthyroidism in Pregnancy; Pregnancy Related Complications.

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Introduction

Thyroid disorders are the second most common endocrinology disorder found in pregnancy. Overt hypothyroidism is estimated to occur in 0.3-0.5% of pregnancies. Subclinical hypothyroidism appears to occur in 2-3%, and hyperthyroidism is present in 0.1-0.4% [1]. Postpartum thyroiditis (PPT) reportedly affects 4-10% of women. PPT is an autoimmune thyroid disease that occurs during the first year after delivery. Women with PPT present with transient thyrotoxicosis, hypothyroidism, or transient thyrotoxicosis followed by hypothyroidism. This presentation may be unrecognized, but is important because it predisposes the woman to develop permanent hypothyroidism [2]. Hypothyroidism during pregnancy has an adverse effect on both mother and child. Children born to untreated or undertreated mothers have profound effect on future intellectual development [3]. Pregnancy has a profound physiological impact on the thyroid gland and thyroid function. During pregnancy, the thyroid gland increases in size by 10% in iodine sufficient countries and to a greater extent in iodine deficient countries [4]. Production of thyroid hormones and iodine requirement both increases by approximately 50% during pregnancy as part of physiology [5]. In addition, pregnancy is a stressful condition for the thyroid gland resulting in hypothyroidism in women with limited thyroid reserve or iodine deficiency.The prevalence of hypothyroidism in pregnancy is around 2.5% according to the Western literature [6]. There are a few reports of prevalence of hypothyroidism during pregnancy from India with prevalence rates ranging from 4.8% to 11% [7,8].

The physiological changes of pregnancy can simulate thyroid disease. Symptoms of heat intolerance, sluggishness, fatigue, and constipation and examination findings of tachycardia, edema, and wide pulse pressure are common to pregnancy and thyroid disease much in same way [9]. The prevalence of overt hyperthyroidism complicating pregnancy has been reported to range between 0.4 and 1.7% [10] and an estimated 2–3 % of women are hypothyroid during pregnancy [11]. Women with thyroid dysfunction both overt and subclinical are at increased risk of pregnancy-related complications such as threatened abortion, preeclampsia, preterm labor, placental abruption, and postpartum hemorrhage. Fetal complications include low-birth-weight, first-trimester spontaneous abortions, preterm birth, fetal or neonatal hyperthyroidism, intrauterine growth retardation, high rates of still birth and neonatal deaths, neonatal hyperbiliru-binemia, higher incidence of neonatal hypothyroidism, and increased perinatal mortality [12].

Hence the present study was done at our tertiary care centre to assess the prevalence of thyroid disorders in pregnant women and to observe the obstetric outcomes of these women suffering from thyroid disorders.

Materials and Methods

The present prospective analytical study was conducted among pregnant women to assess the prevalence of thyroid disorders among them and to observe the obstetric outcomes of these women suffering from thyroid disorders. The study was conducted between May 2015 to May 2017. Considering a confidence level of 95% and confidence interval of 3.1 the number of patients in our study to achieve statistical significance was calculated to be 999. Hence a sample size of 1000 was considered adequate for our study.All healthy singleton pregnant women (primigravida/Multigravida of any age) visiting the department for first visit were selected for the study after taking informed consent while pregnancies with multifetal gestation, history of previous bad obstetric history with known cause, known case of metabolic disorder and who failed to follow up for antenatal care and delivery were excluded from the study. A detailed clinical history, menstrual history, obstetric history, past history medical history, family history, and personal history was taken. General physical examination, Systemic examination was done and findings were noted. Per abdomen examination and USG was done to confirm pregnancy and fetal well-being.Patients were sent for TSH testing. If TSH deranged was observed then FT3 and FT4 levels were checked and patients were diagnosed according to test results and further medical management was done.

According to American Thyroid Association guidelines, normal TSH level is 0.1–2.5, 0.2–3, 0.3–3 milli IU/L in first, second and third trimesters respectively same as normal range of Free T3 is 2.11–3.83, 1.96–3.38, 1.96–3.38 pg/ml and normal range of Free T4 is 0.70–2.00, 0.50–1.60, 0.50–1.60 ng/dl in first, second and third trimester respectively and these values were taken as reference for this study. Every 8 week TSH level was estimated and the dose of the drug was adjusted. At the end, the obstetric and perinatal outcome of the pregnancy was noted.

Quantitative data is presented with the help of Mean and Standard deviation. Comparison among the study groups is done with the help of unpaired t test as per results of normality test. Qualitative data is presented with the help of frequency and percentage table. Association among the study groups is assessed with the help of Fisher test, student t test and Chi-Square test. 'p' value less than 0.05 is taken as significant. Appropriate statistical software, including but not restricted to MS Excel, SPSS ver. 20 are used for statistical analysis. Graphical representation is done in MS Excel 2010.

Results

In the present study, 62 out of 1000 pregnant women screened had thyroid disorders. The prevalence of thyroid disorders in our study was 6.2%. The prevalence of subclinical hypothyroidism, overt hypothyroidism, subclinical hyperthyroidism and hyperthyroidism was 3.6%, 1.6%, 0.8% and 0.2% respectively (Table 1).The mean age of subclinical hypothyroid and overt hypothyroid patients was 24.5±2.41 and 27.1±2.25 years respectively while the mean age of subclinical hyperthyroid and overt hyperthyroid patients was 26.1±6.27 and 30.5±2.12 years respectively. The mean age of euthyroid patients was 24.4±2.43 years. The maternal age was significantly high in the overt hypothyroid (p=0.0006) and overt hyperthyroid groups (p=0.0015) (Table 2). Majority of the patients in all the groups were primigravida. There was no statistically significant difference between the groups with respect to parity and Socioeconomic status (p>0.05) (Table 3). It was observed that there were significantly more cases in 1st trimester in Subclinical hypothyroid group. There was statistically significant difference between the groups with

respect to Trimester wise distribution (p=0.0001) (Table 3). 75.1% of subclinical hypothyroid, 37.6% of overt hypothyroid, 87.5% of subclinical hyperthyroid, 50% of overt hyperthyroid and 76.6% of euthyroid patients had Normal Vaginal Delivery (NVD). The rate of caesarean section was significantly higher in patients with overt hypothyroidism (43.7% vs. 21.1% p=0.0287) as compared to the euthyroid group. Spontaneous abortion was significantly more in overt hypothyroidism group (p=0.0004) (Table 4). Subclinical hypothyroidism was significantly associated with preeclampsia (22.2% vs. 7.8%, p=0.0021) as compared to the euthyroid patients. Adverse maternal effects in overt hypothyroidism included preeclampsia (18.7% vs. 7.8%) and placental abruption (18.7% vs. 0.8%, p=0.0001) (Table 5).

Adverse fetal outcomes in overt hypothyroidism included premature birth (37.5% vs. 5.8%, p=0.0003), intrauterine growth retardation (25% vs. 4.9%, p=0.0174), low birth weight (50% vs. 12.1% p=0.009), fetal distress (18.7% vs. 2.3%, p=0.0036), stillbirth (18.7% vs. 1.7%, p=0.0037) and NICU admission (25% vs. 4.6%, p=0.0134) as compared to the euthyroid patients. All outcomes were found to be highly significant. Adverse fetal outcomes in subclinical hypothyroidism included premature birth (11.1% vs. 5.8%), intrauterine growth retardation (8.3% vs. 4.9%), low birth weight (25% vs. 12.1%), fetal distress (5.5% vs. 2.3%), still birth (2.7% vs. 1.7%) and NICU admission (2.7% vs. 4.6%, p>0.05) as compared to the patients (Table 6).It was observed that respiratory distress syndrome was

Table 1: Distribution of patients as per Thyroid Function Test Results

Thyroid Status	N	%
Subclinical Hypothyroid	36	3.6%
Overt Hypothyroid	16	1.6%
Subclinical Hyperthyroid	8	0.8%
Overt Hyperthyroid	2	0.2%
Euthyroid	938	93.8%
Total	1000	100%

Table 2: Distribution of patients according to Age

Age (yrs)	Subclinical Hypothyroid		Overt Hypothyroid		Subclinical Hyperthyroid		Overt Hyperthyroid		Euthyroid		Chi-Square
	N	%	N	%	N	%	N	%	N	%	
≤20	3	8.3%	0	-	1	12.5%	0	-	32	3.4%	3.325
21-25	22	61.2%	4	25%	5	62.5%	0	-	613	65.3%	
26-30	11	30.5%	11	68.8%	0	-	1	50%	283	30.2%	
>30	0	-	1	6.2%	2	25%	1	50%	10	1.1%	
Total	36	100%	16	100%	8	100%	2	100%	938	100%	
Mean± SD	24.5±2.41		27.1±2.25[a]		26.1±6.27		30.5±2.12[b]		24.4±2.39		

Table 3: Distribution of patients according to various parameters

Variables		Sub clinical Hypo thyroid		Overt Hypothyroid		Sub clinical Hyper thyroid		Overt Hyper thyroid		Euthyroid		p Value
		N	%	N	%	N	%	N	%	N	%	
Parity	Primigravida	20	55.6%	9	56.3%	5	62.5%	1	50%	655	69.8%	>0.05
	Multi gravida	16	44.4%	7	43.7%	3	37.5%	1	50%	283	30.2%	
	Total	36	100%	16	100%	8	100%	2	100%	938	100%	
Socio-economic class	Lower	4	11.1%	1	6.2%	1	12.5%	0	-	93	9.9%	>0.05
	Middle	25	69.5%	12	75.1%	5	62.5%	2	100%	675	72%	
	Upper	7	19.4%	3	18.7%	2	25%	0	-	170	18.1%	
	Total	36	100%	16	100%	8	100%	2	100%	938	100%	
Trimester	1st (n=334)	26	72.2%	10	62.7%	5	62.5%	2	100%	291	31.1%	<0.05
	2nd (n=333)	6	16.7%	4	25%	2	25%	0	-	321	34.2%	
	3rd (n=333)	4	11.1%	2	12.3%	1	12.5%	0	-	326	34.7%	
	Total	36	100%	16	100%	8	100%	2	100%	938	100%	

significantly present in neonates of overt hypothyroid group (p=0.0023). No other significant neonatal complications were seen in terms of hyperbilirubinemia, respiratory distress syndrome, sepsis, hypoglycemia, hypothermia, intracranial bleed, necrotizing enterocolitis and early neonatal death in different groups (Table 7).

Discussion

It is best to screen women early in the pregnancy for thyroid dysfunction because they are common, treatable, and to some extent preventable conditions which produce morbidity and pose special risks for

Table 4: Distribution of patients according to Mode of Delivery

Mode of Delivery	Subclinical Hypothyroid		Overt Hypothyroid		Subclinical Hyperthyroid		Overt Hyperthyroid		Euthyroid	
	N	%	N	%	N	%	N	%	N	%
Vaginal Delivery	27	75.1%	6	37.6%	7	87.5%	1	50%	718	76.6%
LSCS	7	19.4%	7	43.7%	1	12.5%	1	50%	198	21.1%
Abortions	2	5.5%	3	18.7%	0	-	0	-	22	2.3%
Total	36	100%	16	100%	8	100%	2	100%	938	100%

Table 5: Maternal Complications in patients

Maternal Complications	Subclinical Hypothyroid		Overt Hypothyroid		Subclinical Hyperthyroid		Overt Hyperthyroid		Euthyroid	
	N	%	N	%	N	%	N	%	N	%
Anemia	0	-	0	-	0	-	0	-	0	-
Preeclampsia	8	22.2%	3	18.7%	0	-	0	-	73	7.8%
Abruption	0	-	3	18.7%	0	-	0	-	8	0.8%
GDM	0	-	1	6.2%	0	-	1	50%	5	0.5%
PPH	2	5.5%	1	6.2%	0	-	0	-	50	5.3%
Preterm Delivery	3	8.3%	2	13.4%	0	-	0	-	63	6.6%
Oligohydraminos	2	5.5%	1	6.2%	0	-	0	-	13	1.3%

Table 6: Fetal Outcomes among patients

Fetal Outcomes	Subclinical Hypothyroid		Overt Hypothyroid		Subclinical Hyperthyroid		Overt Hyperthyroid		Euthyroid	
	N	%	N	%	N	%	N	%	N	%
Premature birth	4	11.1%	6	37.5%[a]	0	-	0	-	54	5.8%
IUGR	3	8.3%	4	25%[b]	0	-	0	-	46	4.9%
LBW	9	25%	6	50%[c]	0	-	0	-	113	12.1%
Fetal distress	2	5.5%	3	18.7%[d]	0	-	0	-	22	2.3%
IUD	1	2.7%	3	18.7%[e]	0	-	0	-	16	1.7%
NICU Admission	1	2.7%	4	25%[f]	0	-	0	-	44	4.6%

Table 7: Neonatal Outcomes among patients

Neonatal Outcomes	Subclinical Hypothyroid		Overt Hypothyroid		Subclinical Hyperthyroid		Overt Hyperthyroid		Euthyroid	
	N	%	N	%	N	%	N	%	N	%
Hyperbilirubinemia	4	11.1%	4	25%	2	25%	0	-	57	6.1%
Respiratory distress syndrome	4	11.1%	4	25%[a]	0	-	0	-	34	3.6%
Sepsis	1	2.7%	2	12.5%	0	-	0	-	8	0.8%
Hypoglycemia	1	2.7%	0	-	0	-	0	-	8	0.9%
Hypothermia	1	2.7%	0	-	0	-	0	-	5	0.5%
Intracranial bleed	0	-	0	-	0	-	0	-	5	0.5%
Necrotising enterocolitis	0	-	0	-	0	-	0	-	2	0.2%
Early neonatal death	1	2.7%	1	6.2%	0	-	0	-	5	0.5%

pregnancy and the developing fetus. Pregnancy induced physiological changes exacerbate or improve thyroid disorders. Milder forms of hypo or hyper dysfunctions will not render women infertile but still associated with miscarriage. The prevalence of thyroid disorders in our study was 6.2%. The prevalence of subclinical hypothyroidism, overt hypothyroidism, subclinical hyperthyroidism and hyperthyroidism in present study and its comparison with findings from other studies is given in table number 8.

Table number 8 shows comparison between mean age among various groups in various studies. The maternal age was significantly high in the overt hypothyroid (p=0.0006) and overt hyperthyroid groups (p=0.0015). Sreelatha S et al. [15] reported 49%of pregnant women in the age group 25-30 yearshad Thyroid disorder.

In the present study, majority of the patients in all the groups were primigravidas. There was no statistically significant difference between the groups with respect to parity (p>0.05). Manju VK et al. [14] descriptive study found majority of the patients were Primi gravida 262 cases (58.4%), Gravida-2 was 113 (25.1%) and >G3 was 74 (16.4%) cases. Sreelatha S et al. [15] reported that 49% of primigravida and 51% multigravidas presented with thyroid disorder.In the present study, 75.1% of subclinical hypothyroid, 37.6% of overt hypothyroid, 87.5% of subclinical hyperthyroid, 50% of overt hyperthyroid and 76.6% of euthyroid patients had Vaginal Delivery. The rate of caesarean section was significantly higher in patients with overt hypothyroidism (43.7% vs. 21.1% p=0.0287) as compared to the euthyroid group. Spontaneous abortion was significantly more in overt hypothyroidism group (p=0.0004). Nangia AS et al. [16] reported 79.3% of euthyroid, 78% of subclinical hypothyroid, 41.6% of overt hypothyroid, 100% of subclinical hyperthyroid, and 50% of overt hyperthyroid patients had normal vaginal delivery. It was observed in our study that there were significantly more cases in 1st trimester in Subclinical hypothyroid group. There was statistically significant difference between the groups with respect to Trimester wise distribution (p=0.0001).In our study, subclinical hypothyroidism was significantly associated with preeclampsia (22.2% vs. 7.8%, p=0.0021) as compared to the euthyroid patients. No significant increase in placental abruption (0% vs. 0.8%), gestational diabetes mellitus (0% vs. 0.5%), postpartum hemorrhage (5.5% vs. 5.3%), preterm delivery (8.3% vs. 6.6%) and oligohydraminos (5.5% vs. 1.3%) was seen in the subclinical hypothyroid patients. Adverse maternal effects in overt hypothyroidism included preeclampsia (18.7% vs. 7.8%) and placental abruption (18.7% vs. 0.8%, p=0.0001). No significant increase in gestational diabetes mellitus (6.2% vs. 0.5%), postpartum hemorrhage (6.2% vs. 5.3%), preterm delivery (13.4% vs. 6.6%) and oligohydraminos (6.2% vs. 1.3%) was seen in the overt hypothyroid group.

In a study by Sahu MT et al. [17] on overt and subclinical thyroid dysfunction among Indian pregnant women reported that significant adverse effects on maternal and fetal outcome were seen emphasizing the importance of routine antenatal thyroid screening. Manju VK et al. [14] in their study reported that preeclampsia and miscarriage were the most common complications found associated with thyroid dysfunction 47 patients each (10.5%). Prolonged period of infertility, recurrent abortions, abruption, post-partum hemorrhage were found significantly high in overt hypothyroidism than others. Saraladevi R et al. [13] in their study reported that the incidence of maternal complications in the cases of subclinical hypothyroidism was preeclampsia (9.37%), preterm delivery (7.81%), abortions (4.68%) and abruption placenta (1.56%). In the present study, the incidence of fetal complications

Table 8: Comparison between prevalence of thyroid disroders among various studies

Sr. No	Variable	Authors	Hypothyroidism	Hyperthyroidism
1	Prevalence of thyroid disorders	Present study	Subclinical: 3.6% Overt: 1.6%,	Subclinical: 0.8% Overt: 0.2%
		Saraladevi R et al[13]	Subclinical: 6.4% Overt: 2.8%	Subclinical: 1.8% Overt: 0.6%
		Manju VK et al[14]	Subclinical: 72.2% Overt: 20.7%	Subclinical: 1.3% Overt: 5.3%
2	Mean age of presentation	Present study	Subclinical: 24.5±2.41 Overt: 27.1±2.25	Subclinical:26.1±6.27 Overt: 30.5±2.12
			Euthyroid: 24.4±2.43 years	
		Manju VK et al[14]	Subclinical: 20-25 years Overt: >35yrs	----

in the cases of subclinical hypothyroidism was IUGR (6.25%), low birth weight (4.68%) and still birth (1.56%). Incidence of maternal complications in 116 pregnant women with thyroid disorders Preeclampsia (10.34%), Abortion (8.62%), Preterm delivery (7.75%), and abruptio placenta (1.72%).

In the present study, adverse fetal outcomes in overt hypothyroidism included premature birth (37.5% vs. 5.8%, p=0.0003), intrauterine growth retardation (25% vs. 4.9%, p=0.0174), low birth weight (50% vs. 12.1% p=0.009), fetal distress (18.7% vs. 2.3%, p=0.0036), stillbirth (18.7% vs. 1.7%, p=0.0037) and NICU admission (25% vs. 4.6%, p=0.0134) as compared to the euthyroid patients. All outcomes were found to be highly significant. Adverse fetal outcomes in subclinical hypothyroidism included premature birth (11.1% vs. 5.8%), intrauterine growth retardation (8.3% vs. 4.9%), low birth weight (25% vs. 12.1%), fetal distress (5.5% vs. 2.3%), still birth (2.7% vs. 1.7%) and NICU admission (2.7% vs. 4.6%, $p > 0.05$) as compared to the patients.Nangia AS et al. [16] observed that adverse fetal outcomes in overt hypothyroidism were spontaneous abortion (16.6 vs. 2.39%, $p = 0.054$), preterm birth (33.3 vs. 5.8%, $p = 0.04$), low birth weight (50 vs. 12.11 %), intrauterine growth retardation (25 vs. 4.9%, $p = 0.02$), and fetal death (16.6 vs. 1.7%, $p = 0.024$) as compared to the euthyroid women. All of them were found to be highly significant. Adverse fetal outcomes in subclinical hypothyroidism included spontaneous abortion (5.5 vs. 2.39%), preterm delivery (11.2 vs. 5.8%), low birth weight (25 vs. 12.11%), and intrauterine growth retardation (8.4 vs. 4.9%) as compared to the euthyroid women. Preterm birth was found to be statistically significant ($p = 0.02$).

It was observed in our study that respiratory distress syndrome was significantly present in neonates of overt hypothyroid group (p=0.0023). No other significant neonatal complications were seen in terms of hyperbilirubinemia, respiratory distress syndrome, sepsis, hypoglycemia, hypothermia, intracranial bleed, necrotizing enterocolitis and early neonatal death in different groups. Nangia AS et al. [16] reported no significant difference in terms of NICU admission, Apgar score<7 at 5 min, and neonatal complications needing admission to NICU, except respiratory distress syndrome which was seen significantly in patients with overt hypothyroidism (P<0.005). Le Beau SO et al. [18] study on thyroid disorders during pregnancy reported complications like miscarriage, growth restriction, preterm labor, meconium stained amniotic fluid and increased perinatal mortality. In women who had started thyroxine in pregnancy for subclinical hypothyroidism, the medication can be stopped after delivery and thyroid balance reassessed again after 6 weeks and decision taken regarding continuation of treatment. Serum T3, T4 levels rise 30 minutes after delivery and persist for 5 days. This is due to TSH elevation caused be the stress of delivery. So new born screening should be done from cord blood immediately after delivery or 5 days after delivery.

Conclusions

Thyroid dysfunction is a condition that should be treated aggressively and affects a significant number of women during pregnancy associated with adverse maternal outcome. Thyroid dysfunction is arising in India with recent studies highlighting tremendous increase in incidence. The result of the present study indicates that thyroid dysfunction has got many adverse effects on pregnancy especially if not detected and treated timely. Hence, it is important to screen all pregnant women in the first antenatal visit itself in order to facilitate early diagnosis. They should be properly counseled regarding the adverse outcome of the disease.

Due to the immense impact that the maternal thyroid disorder has on maternal and fetal outcome, prompt identification of thyroid disorders and timely initiation of treatment is essential. Thus, universal screening of pregnant women for thyroid disorder should be considered especially in a country like India where there is a high prevalence of undiagnosed thyroid disorder.

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