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Original article

Study of thyroid disorders on maternal outcome in a rural tertiary care hospital

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ABSTRACT

Background: Thyroid disorders are common problem in pregnant women. Because of complex hormonal changes, hypermetabolic state and nonspecific symptoms during pregnancy, thyroid disorders are often go undiagnosed. Untreated thyroid disorders may lead to adverse maternal outcomes.

Material and Methods: Serum thyroid-stimulating hormone (TSH) testing was done in 514 women enrolled, between 12 to 18 weeks of pregnancy. Free T4 and free T3 were tested in subjects with a deranged TSH value. Subjects were followed up till delivery, and maternal complications related to thyroid dysfunction were studied.

Results: Out of 514 subjects, 64 (12.45%) had deranged thyroid function. Prevalence of overt hypothyroidism was 2.34% and 9.54% had subclinical hypothyroidism. The prevalence of hyperthyroidism was 0.58%. The most significant maternal complications in subjects with hypothyroidism were anemia and preterm delivery (p=0.0001 and 0.0001, respectively), when compared to subjects with euthyroidism.

Conclusions: The occurrence of thyroid disorders was high in present study with associated adverse maternal outcomes. Routine antenatal screening and proper management for thyroid dysfunction is recommended to prevent adverse maternal outcomes.

Keywords: Thyroid dysfunction, Maternal outcome

INTRODUCTION

Among the endocrine disorders in pregnant women, the most frequently encountered are the thyroid disorders Due to the nonspecific symptoms and hypermetabolic state of normal pregnancy, thyroid dysfunction may be overlooked in antenatal period.[1]

Human chorionic gonadotropin (hCG) level is high during the first trimester and that acts like thyrotropin (TSH) (α subunit of hCG and TSH is similar). So, under the influence of placental hCG, the range of TSH is decreased during pregnancy with the lower normal TSH level being poorly defined and an upper limit of 2.5 μIU/L in the first trimester. Tha plasma level of hCG begins to decline to act like TSH at 10-12 weeks of gestation, so TSH is increased a little to an upper normal limit of 3μIU/L in the second and third trimester.[2]

Subclinical hypothyroidism is characterized by elevated serum thyrotropin levels (TSH) and normal free serum thyroxine (T4) concentration, which is one end of spectrum of thyroid disorders.[3]

Effect of subclinical hypothyroidism on pregnancy is not clear and well studied. Higher risk of obstetrical and perinatal adverse

outcomes such as first trimester abortions, placental abruption, gestational hypertension, preterm labor and low birth weight have been cited in literature.[3]

There is a scarcity of studies in literature showing the prevalence of overt and subclinical thyroid dysfunction in pregnant women and its effect on the maternal outcomes in detail. Also, there is a paucity of data and studies in rural population of central India. Hence, our study is a determined attempt to elucidate the topic.

MATERIAL AND METHODS

The Observational, prospective study was carried out in the Department of Obstetrics and Gynaecology, Acharya Vinoba Bhave Rural Hospital of Jawaharlal Nehru Medical College, Sawangi-Meghe, Wardha, Maharashtra, India, over a period of 2 years. The study was conducted after clearance from the institutional ethics committee.

Antenatal cases coming to OPD between 12-18 weeks of gestation were included in the study. Total of 514 cases were studied. Their follow up till delivery was continued.

Subjects with known thyroid disorder were excluded from the study.

After a detailed history and examination, a screening for thyroid disorder was done with serum TSH assay. Subjects with abnormal TSH levels were subjected to FT4 and FT3 estimation.

The reference range used in the study was based on the guidelines of the American Thyroid Association, 2011, for the diagnosis and management of thyroid disease during pregnancy and postpartum period.[4] According to the guidelines, the following reference ranges are recommended; first trimester, 0.1–2.5 μIU/mL; second trimester, 0.2–3.0 μIU/mL and third trimester, 0.3–3.0 μIU/μIL. TSH was assayed by VIDAS based on the ELFA (Enzyme Linked Fluorescent Assay) technique.

Subjects were followed up and pregnancy outcomes were noted in terms of pre-eclampsia, anaemia, preterm delivery, abruptio placenta, oligo/polyhydramnios,and mode of delivery.

Biostatical analysis

Statistical analysis was done using descriptive and inferential statistics. Tests used for analysis were Chi Square Test, Z Test and Odd's Ratio.

The results were analysed by using software SPSS 17.0 version and results were tested at 5% level of significance and Graph pad prism 5.0 version.

P value of <0.05 was considered as significant.

Definitions

- Pre-eclampsia was defined as persistently elevated blood pressure (systolic ≥140 mmHg and diastolic ≥90 mmHg) on two or more occasions with proteinuria, after 20th week of pregnancy with previously normotensive and nonproteinuric women.
- Anaemia was defined as maternal haemoglobin contraction in peripheral blood <11 gm/dl.
- Abruptio placenta was defined as a form of antepartum hemorrhage where the bleeding occurs due to premature separation of normally situated placenta.
- Preterm delivery was defined as delivery before 37 completed weeks of gestation.
- Oligohydramnios was defined as condition where the liquor amnii is deficient in amount to the extent of less than 200 ml at term or sonographically amniotic fluid index is <5 cm.
- Polyhydramnios was defined as a state where liquor amnii exceeds 2000 ml or sonographically when amniotic fluid index is >24 cm.

RESULTS

Total of 514 subjects were included in the study. Out of them 64 had deranged thyroid function. Thus, in present study, the prevalence of thyroid dysfunction was 12.45%. Prevalence of overt hypothyroidism

was 2.34%, subclinical hypothyroidism was 9.54% and hyperthyroidism was 0.58%.

Mean TSH level in euthyroid subjects was 1.53±0.58 µIU/L, in subclinical hypothyroid subjects it was 4.95±3.51, in overt hypothyroid subjects it was 6.13±2.31 and in hyperthyroid subjects it was 0.06±0.05.

Table 1: Distribution of study population according to thyroid status

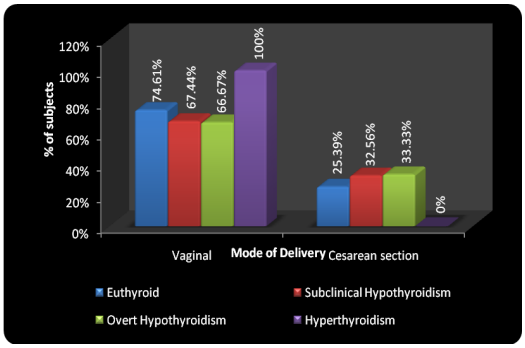
Thyroid status	n	%	Mean TSH Levels (µIU/L)
Euthyroid	450	87.54	1.53
Subclinical Hypothyroidism	49	9.54	4.95
Overt Hypothyroidism	12	2.34	6.13
Hyperthyroidism	3	0.58	0.06
Total	514	100.00	1.96
155.44, p=0.0001, S, p<0.05			

Table 2: Correlation of thyroid status with parity

Parity	Euthyroid Subjects		Subjects with Thyroid dysfunction		Total	
	n	%	n	%	N	%
Primigravida	203	45.11	29	45.31	232	45.14
Gravida 2	147	32.67	21	32.81	168	32.68
Gravida 3	68	15.11	9	14.06	77	14.98
Gravida ≥4	32	7.11	5	7.81	37	7.20
Total	450	100	64	100	514	100
ϰ2-value	0.08,p=0.99, Not Significant					

Table 2 shows that 45.11% of euthyroid subjects and 45.31% subjects with thyroid dysfunction were primigravida, 32.67% of euthyroid and 32.81% of the subjects with thyroid dysfunction were gravida 2, 15.11% of euthyroid and 14.06% of subjects with thyroid dysfunction were gravida 3 and 7.11% of the euthyroid subjects and 7.81% of with thyroid dysfunction were gravida ≥4. By using chi square test statistically no significant difference was found in both the groups (ϰ2-value=0.08, p=0.99, Not Significant).

Graph 1: Correlation of Thyroid status with Mode of delivery



Graph 1 shows that 74.61% of euthyroid subjects, 67.44% of subjects with subclinical hypothyroidism, 66.67% of subjects with overt hypothyroidism and 100% of subjects with hyperthyroidism had vaginal deliveries where as 25.39% of euthyroid subjects, 32.56% of subjects with subclinical hypothyroidism and 33.33% of subjects with overt hypothyroidism had Cesarean Section. Cesarean Section was 1.38 times more in subjects with thyroid disorders as compared to euthyroid subjects. (Odd's-ratio=1.38)

Table 3: Correlation of Thyroid status with adverse maternal outcomes

Maternal Outcome	Euthyroid		Subclinical Hypothyroidism		Overt Hypothyroidism		Hyperthyroidism		ϰ2-value, p-value
	n	%	n	%	n	%	n	%	
Preterm delivery	34	10.52	6	13.95	2	33.33	0	0.00	18.25, 0.0001,S
Anemia	59	18.26	10	23.25	5	55.99	1	100.00	38.97, 0.0001,S
Preeclampsia	26	8.04	5	11.62	1	11.11	0	0.00	0.93, 0.62,NS
Oligohydramnios	20	6.19	2	4.65	0	0.00	0	0.00	5.85, 0.05,NS
Polyhydramnios	1	0.31	1	2.32	1	11.11	0	0.00	16.56, 0.0003,S
Abruptio placentae	2	0.62	1	2.32	1	11.11	0	0.00	13.64, 0.011,S
ϰ2-value	28.24,p=0.0017, Significant, p<0.05								

Table 3 shows that 10.52% out of 343 euthyroid subjects, 13.95% out of 43 subjects with subclinical hypothyroidism and 33.33% out of 9 subjects with overt hypothyroidism had preterm deliveries (p=0.0001,S).

18.26% of euthyroid subjects, 23.25% of subjects with subclinical hypothyroidism and 55.99% of subjects with overt hypothyroidism had anemia (p=0.0001,S).

8.04% of euthyroid subjects, 11.62% of subjects with subclinical hypothyroidism and 11.11% of subjects with overt hypothyroidism had Preeclampsia (p=0.62, NS).

6.19% of euthyroid subjects, 4.65% of subjects with subclinical hypothyroidism had oligohydramnios (p=0.05, NS).

0.31% of euthyroid subjects and 2.32% and 11.11% of subjects with subclinical hypothyroidism and overt hypothyroidism, respectively had polyhydramnios (p=0.0003, S).

0.62% of euthyroid subjects, 2.32% of subjects with subclinical hypothyroidism and 11.11% of subjects with overt hypothyroidism had Abruptio placentae (p=0.011, S).

Subjects with Hyperthyroidism were not included in the study at the time of statistical analysis as there was only one case. Maternal outcome of the subjects who were lost to follow up/yet to be delivered/had miscarriage was not recorded.

DISCUSSION

Thyroid dysfunction is a treatable condition which can produce morbidity and pose special risks during pregnancy. Screening for thyroid dysfunction is important in pregnant women because lack of early diagnosis increases the risk of complications. Maternal thyroid disorders are associated with adverse outcomes in pregnancy, including pregnancy-induced hypertension, anaemia, preterm delivery, placental abruption etc.

In present study, euthyroid subjects were 87.55% and subjects with thyroid disorders were 12.45%. Out of all the subjects with thyroid dysfunction, 9.54% had subclinical hypothyroidism, 2.34% had overt hypothyroidism and and 0.58% had hyperthyroidism.

Similar results of incidence of subclinical hypothyroidism were found by Neelam Aggarwal *et al*[3] (10.9%), Sapana Shah *et al* [5] (9%) and Pandit Vinodh Bandela *et al*[6] (10%). Fakhrolmolouk Yassaee *et al*[2] in their study found that 4.15% had subclinical hypothyroidism and 0.5% had overt hypothyroidism.

However, the prevalence of subclinical hypothyroidism in southern part of India was reported as 0.7%, in study by Thanuja PM *et al*[1].

The discussed variations in the occurrence could be due to different iodide status in the population. Also, other major casuses for thyroid dysfunction among pregnant women in the studied rural population may be poverty and insufficient iodine supplementation.

Statistically, the correlation of parity among women to Thyroid status was insignificant in present study (p=0.99). Similar results were found by Sapana Shah *et al*[5], Neelam Aggarwal *et al*[3] and Weiwei Wang *et al*[7]. However, Pandit Vinodh Bandela *et al*[6] in their study found that 66.9% of all subjects were primigravida, whereas 33.09% were multigravida.

Mean TSH level in euthyroid subjects was 1.53±0.58, in subclinical hypothyroid subjects it was 4.95±3.51, in overt hypothyroid subjects it was 6.13±2.31 and in hyperthyroid subjects it was 0.06±0.05 in present study. Statistically significant variation was found in mean TSH level amongst different groups (p-value=0.0001). Neelam Aggarwal *et al*[3] and Pandit Vinodh Bandela *et al*[6] in their respective studies, found that mean TSH level in subclinical hypothyroid subjects was 6.81±1.1 µIU/ml and 8.15±23 µIU/ml, respectively.

We found that, Cesarean Section was 1.38 times more common in subjects with thyroid disorders as compared to euthyroid

subjects(Odd's ratio =1.38). Similarly, the incidence of caesarean section was significantly higher in hypothyroid group as compared to euthyroid group in study by Neelam Aggarwal *et al*[3] (p=0.001). Likely hood of increased caesarean rate and fetal distress in hypothyroid women may be attributed to the irreversible placental effect of abnormal thyroid status along with TPO antibodies.[3]

In present study we found that 52.84% of subjects with thyroid disorders and 31.88% of euthyroid subjects had abnormal maternal outcome, 47.16% of the subjects with thyroid disorders and 68.12% of euthyroid subjects had normal maternal outcome. By using chi square test statistically significant association was found between maternal outcome and thyroid status of the subjects (ϰ2-value=9.02, p-value=0.002, Significant). Abnormal outcome was 2.39 times more in subjects with thyroid disorders as compared to euthyroid subjects (Odd's Ratio = 2.39).

Anemia (p=0.0001,S) and preterm delivery(p=0.0001,S) were the most common maternal complications in subjects with hypothyroidism in present study. Also, pregnant women with subclinical and overt hypothyroidism had a significant increase in the incidence of polyhydramnios (p=0.0003,S) and Abruptio placentae (p=0.011,S).

In association with structurally defective placentation, the utero placental interface is susceptible to both thrombosis and haemorrhge. Various factors may mediate such pathogenesis, like tissue factor production in response to aberrant vascular endothelial growth factor and inflammatory cytokine release, which promotes thrombosis. Also, shallow extravillous thromboblast invasion could lead to placental ischemia and haemorrhage generating thrombin locally, which in turn mediates the degradation of extracellular matrix. All of this, thus triggers pre-mature placental separation from the uterus.[8]

In the present study, 8.04% of euthyroid subjects, 11.62% of subjects with subclinical hypothyroidism and 11.11% of subjects with overt hypothyroidism had Preeclampsia.

By increasing the number of beta adrenoceptors, thyroid hormones potentiate Beta adrenergic response with an inverse action on alpha adrenergic receptors., The density of alpha-1 adrenoceptors increases in hypothyroid state, while beta adrenoceptors are reduced on vascular beds. Action of alpha adrenoceptors mainly involves smooth muscle cell contraction, causing vasoconstriction in the blood vessel.[8]

Neelam Aggarwal *et al*[3] in their study found that, 12% of subjects with subclinical hypothyroidism had Preeclampsia, 1% of subjects with subclinical hypothyroidism had abruptio placentae. Whereas,16% of subjects with subclinical hypothyroidism had preterm deliveries. The incidence of preterm labor and preeclampsia was similar in both groups (P =>0.05).

Pertinent literature to say now that subclinical hypothyroidism has adverse impact on pregnancy is available. But it is still not clear how thyroid deficiency results in maternal complications.[3]

Although uncommon, the effects of hyperthyroidism in pregnancy on both mother and child are critical. In present study, no significant conclusion could be drawn as only 0.58% subjects had hyperthyroidism.

CONCLUSION

The occurrence of thyroid disorders was significant in present study.

We would like to conclude on the basis of present study, that both subclinical and overt hypothyroidism are significantly associated with adverse maternal outcomes. There are no recommendations available at present in India, for detection of thyroid dysfunction among pregnant women. Recent consensus guidelines recommend testing only in high risk women having personal history of thyroid or other autoimmune disorders or with a family history of thyroid disorders.

Therefore, we recommend, routine antenatal screening and proper management for thyroid

dysfunction to prevent adverse maternal outcomes.

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