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THE STUDY OF MATERNAL AND FETAL OUTCOME IN PREGNANT WOMEN WITH THYROID DISORDER: A PROSPECTIVE STUDY IN INDORE REGION

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ABSTRACT

BACKGROUND: Thyroid disorder is very common disorders in pregnancy. It is well established that overt and subclinical thyroid dysfunction has adverse effects on mother and the foetus like miscarriages, preterm delivery, pre-eclampsia, eclampsia, polyhydramnios, placental abruption, postpartum haemorrhage, low birth weight, fetal distress, NICU admission. 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 carried out in Index Medical College, Indore, MP, India in Department of physiology in collaboration with Department of Obstetrics & Gynecology. It is a prospective random cross-sectional study done over 180 pregnant women (90 pregnant women with thyroid disorder and 90 with normal thyroid) which includes known cases of thyroid disorder. Serum thyroid stimulating hormone (TSH), fT3, and fT4 tests were apart from the routine blood sample investigations as per FOGSI-ICOG good clinical practice recommendation. Patients are followed up till delivery, and their obstetrics and perinatal outcomes are noted.

RESULTS: In our study prevalence of thyroid dysfunction was 10.4%. Out of these 90 patients with thyroid dysfunction, complications associated were pre-eclampsia (14.4%), abortions (13.3%), maternal anaemia (11.1%), preterm labour (7.8%), still birth (5.6%), abruption placenta (4.4%). Out of 90 patients with thyroid dysfunction, foetal complications seen were low birth weight (22.2%), NICU admission (15.6%), hyperbilirubinemia (14.4%) and foetal distress (5.6%).

CONCLUSIONS: Our result demonstrated that the thyroid disorders during pregnancy have adverse effects on maternal and foetal outcome emphasizing the importance of routine antenatal thyroid screening.

KEYWORDS : Hyperthyroidism, Hypothyroidism, Pregnancy, Pregnancy-induced thyroid dysfunction, Thyroid dysfunction

INTRODUCTION:

Thyroid gland plays a major role in pregnancy, and thyroid gland disorders constitute very common endocrine disorders during pregnancy [1]. There are significant and reversible changes in thyroid function during pregnancy. Also there is an enhanced urinary loss of iodine owing to an increased glomerular filtration rate, leading to iodine deficiency and maternal goiter [2]. There is an increase in thyroxine-binding globulin (TBG) because of elevated oestrogen and decrease in the level of thyroid-stimulating hormone (TSH) with an increase in human chorionic gonadotropin concentration [3]. Placenta produces the enzyme deiodinase, which increases the peripheral metabolism of thyroid hormones and regulates the trans-placental transport of thyroid hormone and iodide [4]. In short the thyroid gland is overburden with work during pregnancy which can cause hypothyroidism in women with moderate thyroid hormone reserve or iodine deficiency.

The developing fetus synthesizes thyroid hormones after the 12th week of gestation and depends on mother's thyroid hormone for organogenesis, general growth, and development of the central nervous system.4 Thyroidal hormones (T_3,T_4) are essential for the maintenance and successful completion of normal pregnancy [5].

There are two main clinical forms of hypothyroidism. First is subclinical hypothyroidism, which shows increase serum TSH with normal free thyroxine (FT4) and is observed in 3%–5% of women in pregnancy. Second is overt hypothyroidism, characterized by an increase serum TSH and subnormal FT4 is observed in 0.3%–0.5% of women in pregnancy [6].

Occurrence of hyperthyroidism is less during pregnancy with the prevalence being 0.1%–0.4% [7]. Overt hyperthyroidism is seen in nearly 0.002% of pregnancy characterized by a reduced TSH and an increased FT3/FT4. Subclinical hyperthyroidism is seen in 1.7% of pregnancy and is characterized by a suppressed serum TSH and normal FT4 [8].

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.

MATERIAL & METHODS:

This prospective random cross sectional study was done in the Department of physiology in collaboration with Department of Obstetrics & Gynecology at Index Medical College, Indore, MP, India. A total of 865 pregnant women reported in which 90 were having thyroid dysfunction. Other 90 healthy pregnant women who willing to participate in study and reported to follow-up were randomly selected studied during the study period between of one and half year.

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. Total 865 pregnant women reported to our institution in which 90 women having abnormal thyroid dysfunction. The sample size was 180 patients. The control group (90 pregnant women) includes patients with normal TSH level. The study (90 pregnant women) includes patients with abnormal TSH levels.

The reference range of test values as per American Thyroid Association Guidelines

- TSH during 1st trimester - 0.1 to 2.5mIU/L
  2nd trimester - 0.2 to 3.0mIU/L
  3rd trimester - 0.3 to 3.0mIU/L
- Normal free T4 - 0.7 to 1.8 ng/ml
- Normal free T3 - 1.7 to 4.2 pg/ml

Depending on the normal values, patients were classified into

- Subclinical hypothyroidism : High serum TSH with normal fT4 , fT3 level
- Overt hypothyroidism : High serum TSH with fT4 ,fT3 less than normal
- Subclinical hyperthyroidism : low serum TSH with normal fT3, fT4

- Overt hyperthyroidism : low serum TSH with fT4 & fT3 more than normal range

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 was 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 and5-minute, number of neonatal intensive care unit (NICU) admission, neonatal sepsis, neonatal death and development of congenital hypothyroidism.

STATISTICALANALYSIS

The data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 23 for Windows. Mean along with standard deviation (±SD) was used to describe quantitative data meeting normal distribution. Discrete (categorical) groups was compared by chi-square ($\chi 2$) test was used to correlate demographic distribution in groups. p values less than 0.05 ($p<0.05$) was considered statistically significant.

OBSERVATION:

Out of 865 pregnant women; patients having hypothyroidism with 48 subclinical and 8 overt patients while hyperthyroidism was found in 34 patients with subclinical in 27 and overt on 7. The prevalence of thyroid dysfunction was 10.40% in which hypothyroidism was 6.47% and hyperthyroidism was 3.93%.

The majority of patients were in the age group 31-35 years (36.7 %) followed by 26-30 years age group (22.8%) and the least were of age below 25 years (18.3%). Nearly equal distribution of parity in studied pregnant women. The majority of patients were having the BMI above>30 kg/m2 BMI 39.4% followed by 26-30 kg/m2 (37.8%) while only 22.8%were having 25 kg/m2 BMI. 69.4% pregnant women were belonging from rural area. The majority of patients were from middle class (46.7%) followed by lower middle (31.7%) and the least were of upper class status (3.3%) (Table No. 1).

Majority of patients were of abortion (29) followed by maternal anaemia (15),pre-eclampsia (13) patients, preterm delivery (11) and the least complications were of abruption placenta (4) and IUGR (5) (Table No. 2). The association was found to be statistically significant ($p<0.05$) in the cases of pre-eclampsia and abruption placenta while rest of the complications have shown insignificant association ($p>0.05$) (Table No. 3).

The correlation between normal and thyroid dysfunction in term of fetal complications where fetal 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 No. 4).

Table No. 1: Demographic distribution of studied pregnant women

		Frequency (n=180)	Percentage
Age (Years)	≤25	33	18.3
	26-30	41	22.8
	31-35	66	36.7
	36-40	40	22.2
Parity	Single	91	50.6
	Multiple	89	49.4
BMI (Kg/m^2)	≤25	41	22.8
	26-30	68	37.8
	≥30	71	39.4
Residence Location	Rural	125	69.4
	Urban	55	30.6
Socio-economic status	Lower	13	7.2
	Lower middle	57	31.7
	Middle	84	46.7
	Upper middle	20	11.1
	Upper	6	3.3

Table No. 2: Maternal complication in different thyroid dysfunction

Maternal complication	Normal	Hypothyroidism		Hyperthyroidism		Total (n=180)
		Subclinical	Overt	Subclinical	Overt	
Abortion	17	3	0	5	4	29
Maternal Anaemia	5	10	0	0	0	15
Pre-eclampsia	0	10	0	3	0	13
Preterm delivery	4	0	2	5	0	11
Still Birth	2	0	3	2	0	7
IUGR	5	0	0	0	0	5
Abruption placenta	0	2	0	2	0	4
Total	33/90	25/48	5/8	17/27	4/7	84/180

Table No. 3: Correlation between normal and thyroid dysfunction in term of maternal complication

Complication	Normal	Thyroid Dysfunction	P value
Abortion	17 (18.9%)	12 (13.3%)	0.311
Maternal Anaemia	5 (5.6%)	10 (11.1%)	0.178
Pre-eclampsia	0 (0.0%)	13 (14.4%)	**<0.001**
Preterm delivery	4 (4.4%)	7 (7.8%)	0.351
Still Birth	2 (2.2%)	5 (5.6%)	0.247
UGR	5 (5.6%)	0 (0.0%)	**0.023**
Abruption placenta	0 (0.0%)	4 (4.4%)	**0.043**
Total	33/90	51/90	**0.007**

*** Chi square test/Fishers test**

Table No. 4: Correlation between normal and thyroid dysfunction in term of fetal complication

Fetal Complication	Normal	Thyroid Dysfunction	P value
Low birth weight	4 (4.4%)	20 (22.2%)	**<0.001**
Hyperbilirubinemia	5 (5.6%)	13 (14.4%)	**0.047**
Fetal distress	3 (3.3%)	5 (5.6%)	0.469
NICU admission	5 (5.6%)	14 (15.6%)	**0.029**
Total	17/90	52/90	**<0.001**

*** Chi square test/Fishers test**

DISCUSSION

The most frequent thyroid disorder in pregnancy is maternal hypothyroidism. The geographical variation in prevalence of hypothyroidism during pregnancy is very wide. The range of variation starts from 2.5% in the west to 11% in India [10]. There is predominance in prevalence of hypothyroidism in Asian countries compared with the western countries. Untreated or inadequately treated and subclinical hypothyroidism can increased risk of miscarriage, preeclampsia, anaemia, fetal growth restriction, placental abruption, perinatal and neonatal morbidity and mortality, preterm delivery, small head circumference, low birth weight 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 significant number of them will develop hypothyroidism (TSH >3 mlIU/l) in third trimester and Postpartum thyroiditis [13].

In this study the prevalence of thyroid dysfunction out of 865 reported pregnant women was found to be 10.40% and the comparable results were observed by **Mulik J et al [14], Sahu MT et al [15], Azenabor A [16], Singh A [17], Chunchaiah S et al** [18] past Indian and also these findings in accordance with the world wide investigation.

In the present study the mean age was observed as 31.30±4.92years and similar results were obtained in various past studies as mentioned in the above table i.e. **Azenabor A [16], Abdulslam K et al [19] and Irinyenikan et al [20]** has observed the mean age of the studied patients as 29.82±4.39, 27.7±7.8 and 30.4±4.62 respectively. This implies that 3rd decade of life is the ideal age for pregnancy and among

the patients with gestational hypertension or hypotention.

In this study the prevalence of subclinical hypothyroidism was found to be 5.50% and overt hypothyroidism as 0.92% while subclinical hyperthyroidism was observed as 3.12% and 0.81% overt hyperthyroidism which means that hypothyroidism that too subclinical hypothyroidism is more common in pregnant women than hyperthyroidism. Studies done by **Sahu MT et al [15], Abdulslam K et al [19], Gayathri R [21] and Nazarpour S et al [22]** also reported hypothyroidism as more common than hyperthyroidism.

In the our study the maternal complications in different thyroid dysfunction and majority of patients were of abortion 29 women followed by maternal anaemia15 women, Pre-eclampsia13 patients, 7 cases were of preterm delivery and the least complications were of abruption placenta 4 patients. The association was found to be statistically significant ($p<0.05$) in pre-eclampsia, IUGR and abrution placenta. **Chunchaiah S et al** [18] reported abortion as the most common complication followed by IUGR and others which are similar to our result. **Singh A & Reddy MJ [17], Manju VK and Sathiamma PK [23] and S Sreelatha et al [24]** also reported the similar complications in their respective studies. **PM Thanuja et al** [25] reported the maternal complications included abortion (50%) low birth weight (50%).

Sarkar D [26] in a study found that minimal degree of hypothyroidism can increase the rate of miscarriage and fetal death and can be an underlying etiology of recurrent pregnancy loss.13 Prolonged period of infertility, recurrent abortions, abruption placenta ($p<0.05$), PPROM, preterm labor, post-partum hemorrhage were found significantly high in overt hypothyroidism than others. Normocytic anemia was found significantly high in subclinical hypothyroidism (9.8%) Abdominal delivery was high in overt hypothyroidism. **Shau MT et al** [15]also found complications like abortion, hyperemesis gravidarum, preeclampsia, IUGR and preterm labor to be higher in pregnant women with thyroid disorder as compared to euthyroid pregnant women but did not find this association to be significant statistically ($p>0.05$). **Gupta HP et al** [27] also reported significant association ($p<0.05$) in pre-eclampsia and abruption placenta.

Thyroid disorders have a significant influence over metabolic and physiological activities and hence these eventually affect the maternal and fetal wellbeing.

In this study the correlation between normal and thyroid dysfunction in term of fetal complications where fetal distress was having insignificant association ($p>0.05$) while other complications like Low birth weight, Hyperbilirubinemia and NICU admission were having statistically significant association ($p>0.05$). **Gupta HP et al** [27] reported thyroid disorders have a significant ($p<0.05$) influence over metabolic and physiological activities and hence these eventually affect the maternal and fetal wellbeing.

Prasad DR et al [28] reported 21.4% babies with neonatal hyperbilirubinemia were born to hypothyroid women compared to 16.5% babies born to euthyroid women. This is statistically insignificant ($p<0.05$). Similar to present study, **Ajmani SN et al** [29] 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 ($p<0.05$). **Dhanwal DK et al** [30] also reported significant ($p<0.05$) adverse effects on maternal and fetal outcomes were observed emphasizing the importance of routine antenatal thyroid screening. Therefore, results of our study are consistent with other previously reported data from India. This study also shows a rising trend of hypothyroidism among the Indian pregnant women.

CONCLUSION

In our study prevalence of thyroid dysfunction in pregnant women was found to be 10.40%. Pre-eclampsia, Abortion and UGR were the most common complication found associated with thyroid dysfunction, anemia and recurrent pregnancy loss follows. Low birth weight and Hyperbilirubinemia were the common foetal complications followed by Fetal distress and NICU admission ($p<0.05$). Thyroid dysfunction in pregnancy is associated with adverse maternal and foetal outcomes; hence, antenatal thyroid screening must be done. Maternal hypothyroidism is a disorder which affects both maternal and fetal outcomes and is also associated with multiple other conditions which affect maternal and fetal health. Prompt detection and corrective treatment with thyroxine can prevent many obstetrical complications and result in the delivery of a healthy baby. Therefore, routine testing with serum TSH is a sufficient and cost-effective screening tool.

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