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The Association of Hypothyroidism and Maternal- Fetal Outcome In Tertiary Medical Centre in South Bihar

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Abstract:
Background*: Pregnancy influences thyroid function in multiple ways .Not only does the maternal hypothalamic-pituitary-thyroid (HPT) axis undergo a series of adjustments, the fetus develops its own HPT axis and the placenta plays an active role in iodide and T4 transport and metabolism. Thus, an integrated three-compartment thyroid model exists during gestation.*
Aim and Objectives: *To study the perinatal outcome of hypothyroid pregnant women in comparison to normal pregnant women to look for maternal and fetal complication.*
Materials and Methods*: This prospective study was conducted in department of Obstetrics and Gynecology, Narayan medical college and Hospital, Jamuhar, Sasaram, South Bihar from Oct 2020 to March 2021. All pregnant women attending the obstetric unit during this period were included in the study after informed consent. : Details regarding personal characteristics, demographic data, menstrual cycle, obstetric, family and past history were noted. Emphasis was given on risk factors. A thorough general and physical examination with reference to pulse, BP, temperature and respiratory rate followed by examination of the CVS, CNS, respiratory system and local thyroid examination was done.*
Results: *140(70%) study subjects do not had any maternal complications, with TSH value 3.21±2.81 and 3.04±0.95 in 1st trimester and 2nd trimester respectively. 22% study subjects had PIH, The TSH value of study subjects had PIH was 3.83±2.16 and 3.07±0.79 in 1st and 2nd trimester respectively. 8% subjects had preterm labour having TSH level 4.4±5.16 and 4.01±0.89 in 1st and 2nd trimester respectively. On applying ANOVA test we found 1st trimester TSH was not statistically associated with p value-0.19 , however 2nd trimester TSH is statistically significantly associated with maternal complication. we do not found any significant association in both 1st and 2nd trimester TSH with NICU Admission with p value -0.57 and 0.12 respectively.*
Conclusion: *Early and effective treatment of thyroid disorders ensures safe pregnancy with minimal maternal and fetal complication.*
Key Word*: TSH, NICU, PIH, PROM,PRE-TERM*

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I. Introduction

Hypothyroidism is one of the most common diseases associated with pregnancy. The prevalence of hypothyroidism during pregnancy is reported to be 0.3-0.5% of hypothyroidism and 2-3% of subclinical hypothyroidism.1

Pregnancy affects the thyroid function in many ways. Not only maternal axis of the hypothalamic-pituitary-thyroid (HPT) experience a series of changes, the fetus develops its own HPT axis and the placenta plays a prominent role in the transport of the iodide and metabolism of T4. Therefore, an integrated model is present during pregnancy2

The thyroid gland increases by 10% in size during pregnancy in iodine-rich area and by 20% -40% in iodine-efficient areas. The production of thyroxine (T4) and triiodothyronine (T3) increases by 50% of daily iodine requirement.3

Fetus should only rely on the mother's hormonal system before 12-14 weeks of pregnancy, so maternal hypothyroidism at this stage can cause vascular insufficiency, low IQ, severe mental retardation and impaired growth. Tri-iodothyronin uses the enzymes needed for emotional development so maternal hypothyroidism cannot be left untreated even for the 1st trimester4

Converting hypothyroidism is a complication of 2-3 pregnancies per 1000, while lower extremity disease is seen in about 5% .5

Untreated or over-treated women with hypothyroidism experience 40% of cases of anemia, preeclampsia, placental abruption and post-partum hemorrhage, 30% of neonates in pregnancy and 10% of cases

of births and birth defects have been noted. Women with untreated subclinical hypothyroidism (high TSHonly) had about one-third of the cases, the maternal and child outcomes improved with thyroxine therapy.6

Babies born to women who were not treated for thyroid deficiency during pregnancy (as defined by increased serum TSH) had IQ levels that were 7 points below those in controls.7

Among Hypothyroid women TPO antibodies positivity was detected in 57.1%. No correlation was observed between hypothyroidism or TPO antibody positivity by age or other. Hypothyroid pregnancy indicates a recurrence of miscarriage and premature delivery. Worldwide 20 million people grow up following neurological sequelae due to depletion of intra uterine iodine8.

There has already been controversy among researcher over the inclusion of thyroid function tests among conventional birth tests and their cost compared to the benefit outcomes. Many believe it is helpful .With the following background, the idea for this study was designed. The aim was To study the perinatal outcome of hypothyroid pregnant women in comparison to normal pregnant women to look for maternal and fetal complication.

II. Material and Methods

This prospective study was conducted in department of Obstetrics and Gynecology, Narayan medical college and Hospital, Jamuhar, Sasaram, South Bihar from Oct 2020 to March 2021. All pregnant women attending the obstetricunit during this period were included in the study after informed consent.

INCLUSION CRITERIA:
1. Antenatal women with <12 weeks of gestation.
2. Singleton pregnancy.

EXCLUSION CRITERIA:
1. Antenatal women with multifetal gestation.
2. Pregnant women with chronic disorder like diabetes mellitus and hypertension.
3. Pregnant women of previous bad obstetric history with known cause.
4. Those who underwent surgery for thyroid.

METHOD: Details regarding personal characteristics, demographic data, menstrual cycles, childbirth, family and past history were noted. Emphasis was given on risk factors. Complete and standard physical examinations for, BP, temperature and respiratory function followed by CVS, CNS, respiratory system and thyroid tests were performed. Thyroid function test (TFT) 10 ml blood sample of pregnant women was drawn on the first visit in the first trimester, TFT was tested by serum TSH and FT4 (ELISA) serial analysis. The outcome of pregnancy varies such as miscarriage, premature delivery, IUGR, preeclampsia, anemia, low birth weight, intra-abdominal hemorrhage, antepartum hemorrhage, still birth, postpartum hemorrhage, congenital asphyxia were studied. The neonatal outcome was also studied by studying baby weight, APGAR Score, Nicu admission.

Statistical analysis

Data was analyzed using SPSS version 20 (SPSS Inc., Chicago, IL). Student's *t*-test was used to ascertain the significance of differences between mean values of two continuous variables. In addition, paired *t*-test was used to determine the difference between baseline and 2 years after regarding biochemistry parameters, and this was confirmed by the Wilcoxon test which wasa nonparametric test that compares two paired groups. Chi-square and Fisher exact tests were performed to test for differences in proportions of categorical variables between two or more groups. The level $P < 0.05$ was considered as the cutoff value or significance.

III. Result

Table 1 : Distribution of study subjects as per age

Age group		Frequency	Percent
Valid	<18 yrs	1	.5
	18-25 yrs	37	18.5
	25-35 yrs	142	71.0
	<35 yrs	20	10.0
	Total	200	100.0

Table 1 shows distribution of study subjects as per age. Majority of study subjects , about 71% subjects belongs to 25-35 yrs, 18.5% subjects belongs to 18-25 year, 10% subjects belongs to <35 yrs whereas only 0.5% subjects belongs to <18 year.

Table 2: Distribution of study subjects as per parity

Parity		Frequency	Percent
Valid	Primigravida	112	56.0
	Multigravida	88	44.0
	Total	200	100.0

Table 2 shows distribution of study subjects as per parity. 56% study subjects were primigravida whereas rest 44% study subjects were multigravida.

Table 3: Distribution of study subjects as per Hypotyroidism Prior to Pregnancy.

Hypothyroidism prior to pregnancy		Frequency	Percent
Valid	Yes	54	27.0
	No	146	73.0
	Total	200	100.0

Table 3 shows distribution of study subjects as per hypothyroidism prior to Pregnancy. Only 27% mothers do not had hypothyroidism before pregnancy whereas only 27% study subjects had hypothyroidism prior to pregnancy.

Fig 1: Error graph showing the value of TSH value in 1st and 2nd trimester and FT4

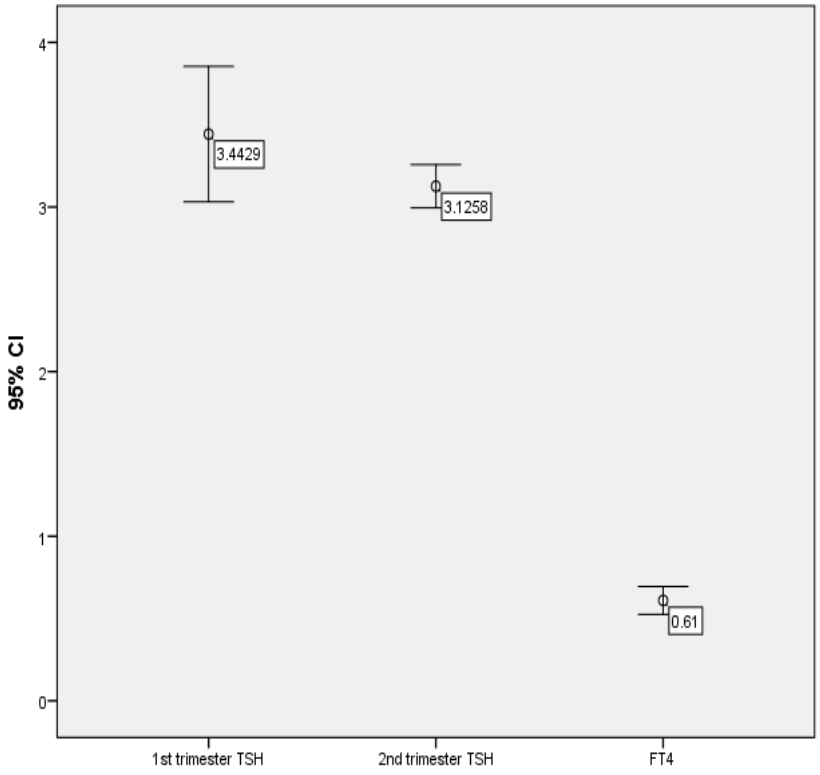

Fig 1 shows Error graph showing the value of TSH value in 1st and 2nd trimester and FT4. The mean value of 1st and 2nd trimester TSH was 3.44 and 3.12 whereas mean of fT 4 was 0.61.

Fig 2 : Correlation of 1st trimester TSH of mother and Baby weight

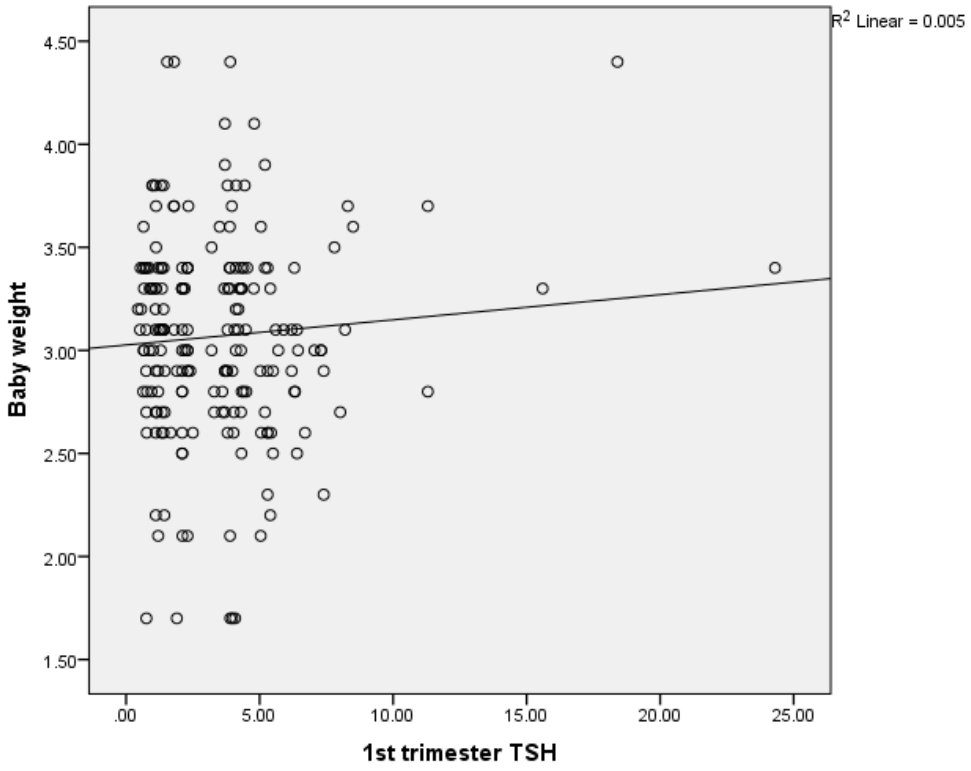

Fig 2 shows Correlation of 1st trimester TSH of mother and Baby weight. On regression analysis we found no correlation between 1st trimester TSH and baby weight with R square 0.005

Table 4 : Correlation of 1st trimester 2nd trimester TSH of mother and mode of termination

mode of termination		1st trimester TSH	2nd trimester TSH
Abortion	Mean	4.5958	3.3583
	N	12	12
	Std. Deviation	2.42239	.92093
Induced vaginal delivery	Mean	2.8441	3.0624
	N	71	71
	Std. Deviation	2.20230	.93724
Spontaneous vaginal delivery	Mean	3.9217	3.0042
	N	48	48
	Std. Deviation	4.09225	.92604
Caeserian Section	Mean	3.6088	3.2375
	N	65	65
	Std. Deviation	2.68626	.99990
Forceps Delivery	Mean	2.1725	3.2000
	N	4	4
	Std. Deviation	2.35408	.00000
		ANOVA test applied F- 1.63, P value- 0.17 Non significant	ANOVA test applied F- 0.48, P value- 0.74 Non significant

Table 4 shows Correlation of 1st trimester, 2nd trimester TSH of mother and mode of termination of pregnancy. It was found that those who undergoes abortion had 1st trimester TSH 4.59±2.42, 2nd trimester TSH 3.35±0.92, whereas those undergoes spontaneous vaginal delivery had 1st trimester TSH 3.92±4.09 and 2nd trimester TSH 3.00±0.92, whereas in caeserian section it was 3.60±2.68, 3.23±0.99, when we apply ANOVA test to assess the correlation in both the 1st and 2nd trimester we found no association, with p value- 0.17 and 0.74 respectively.

IV. Discussion

During the last 20 years, it has been appreciated that thyroid physiology changes significantly during gestation. Uncorrected thyroid dysfunction in pregnancy has adverse effects on fetal and maternal well-being. In this study 200 study subjects were selected. As the primary objective of the study was to look at various maternal and fetal complications with regard to hypothyroidism in pregnancy, important complications observed in this study are listed below.

In the present study Majority of study subjects , about 71% subjects belongs to 25-35 yrs, 18.5% subjects belongs to 18-25 year, 10% subjects belongs to <35 yrs whereas only 0.5% subjects belongs to <18 year. Other study such as by Manisha jain et al1 shows Mean age was 25.9±0.2 for hypothyroid cases and 24.3±0.2 years for euthyroid cases and the difference was statistically significant (p value 0.04). Increased maternal age is associated with increased incidence of hypothyroidism.study by zareen kiran et al9 shows The mean age of the hypothyroid pregnancies was 31 years (SD 4.73). Sreelatha et al10 shows maximum number of pregnant women in the age group 25-30 years who had Thyroid disorder i.e.49%. Least in the age group less than 20 years i.e. 1% and more than 35 years i.e. 2%. 34% women were in the age group 20-25 years who had thyroid disorder.

In the present study 56% study subjects were primigravida whereas rest 44% study subjects were multigravida. Other study such as Sreelatha et al10 had 49% of primigravida and 51% multigravidas with thyroid disorder in their study. Only 27% mothers do not had hypothyroidism before pregnancy whereas only 27% study subjects had hypothyroidism prior to pregnancy.The mean value of 1st and 2nd trimester TSH was 3.44 and 3.12 whereas mean of fT 4 was 0.61. On regression analysis we found no correlation between 1st trimester TSH and baby weight with R square 0.005. A study done by Davis et al6 concluded that perinatal morbidity and mortality was high mainly in women with hypothyroidism and there were frequent low birth weight (31%) babies born .Similar observations were made by Roti et al11among overt hypothyroid mothers not on treatment.It should be noted that in all these studies the reason for low birth weight was stated to be frequent preterm birth and not IUGR .

As the birth weight were almost similar in this study one could probably infer that adequate treatment could improve the neonatal outcomes in terms of birth weight. And in this study the birth weights were comparable due to comparable rates of preterm births among cases and controls. It was found that those who undergoes abortion had 1st trimester TSH 4.59±2.42, 2nd trimester TSH 3.35±0.92, whereas those undergoes spontaneous vaginal delivery had 1st trimester TSH 3.92±4.09 and 2nd trimester TSH 3.00±0.92, whereas in caeserian section it was 3.60±2.68, 3.23±0.99, when we apply ANOVA test to assess the correlation in both the 1st and 2nd trimester we found no association, with p value- 0.17 and 0.74 respectively. A study done by Sharma Partha et al12 reported a caesarean section rate of 29% and Idris et al.13 found an increased rate of Caesarean section 28.7% in cases of treated hypothyroidism as compared to 18% in controls .In another study done by Meenakshi Titoria Sahu et al 14caesarean section rate was significantly higher among pregnant hypothyroid women(p=0.04) .

In this study cesarean section rate among cases (34%) was significantly higher than controls (16%)(p 0.001). The caesarean rate among patients with subclinical hypothyroidism was 10%.But this result had several confounding factors. The study was done at a tertiary hospital receiving patients with high risk pregnancy and among cases 23% had a history of previous caesarean sections. In modern obstetrics labour is monitored with electronic fetal monitoring which also contributes to the increased rates of caesarean sections.

140(70%) study subjects do not had any maternal complications, with TSH value 3.21±2.81 and 3.04±0.95 in 1st trimester and 2nd trimester respectively. 22% study subjects had PIH, The TSH value of study subjects had PIH was 3.83±2.16 and 3.07±0.79 in 1st and 2nd trimester respectively. 8% subjects had preterm labour having TSH level 4.4±5.16 and 4.01±0.89 in 1st and 2nd trimester respectively. On applying ANOVA test we found 1st trimester TSH was not statistically associated with p value-0.19 , however 2nd trimester TSH is statistically significantly associated with maternal complication. Study by Saki F et al15 shows Hypothyroidism was associated with IUGR (P = 0.017) and low Apgar score at first minute (P = 0.04); it increased the risk of IUGR by 2.2 times. Clinical hypothyroidism had no significant association with

preeclampsia (P > 0.05),which is almost similar to our study. Subclinical hypothyroidism had a significant association with IUGR (P = 0.028) and low Apgar score at first minute (P = 0.022).

Davis et al 6 in a study of hypothyroidism complicating pregnancy, found that maternal complications are more common in hypothyroid women with an increase in anemia (31%) and preeclampsia (44%) in them. In a study Roti et al11 found an increased prevalence of maternal complications such as anemia(34%) preeclampsia (46.2%) placental abruption (19%) and fetal complications like low birth weight (31%) fetal death(12%) in LT 4 treated women. Leung et al16 demonstrated a 22% risk of gestational hypertension in pregnant women with overt hypothyroidism which is higher in comparison to euthyroid women. Antolic et al. in 2006 found that mothers treated with LT4, often seem to have preexisting hypertension and preeclampsia compared with healthy women . Wilson KL et al 17 in their study found that women with subclinical hyper- thyroidism who had the lowest TSH levels had an incidence of hypertensive disorders of 6.2%. The association of hypothyroidism and preeclampsia is not surprising. Hypothyroidism is an accepted cause of reversible hypertension both in the pregnant and in the non-pregnant population. Hypothyroidism can cause vascular smooth muscle contraction both in systemic and renal vessels, which leads to increased diastolic hypertension, peripheral vascular resistance, and decreased tissue perfusion. Thyroid dysfunction can be associated with proteinuria, which is known to result in increased excretion of thyroxine and thyroid-binding globulins.

Only 15%(30) study subjects need nicu admission whereas rest 85%(170) study subjects do not need nicu admission. Those who need nicu admission had TSH value 3.72±3.27, 2.88±1.10 in 1st and 2nd trimester respectively whereas those who do not need nicu admission had TSH value 3.39±2.89, 3.17±0.91 in 1st and 2nd trimester respectively. On applying t test we do not found any significant association in both 1st and 2nd trimester with p value -0.57 and 0.12 respectively. Study by Kalpana et al18 shows NICU admission 42.1% was significantly associated with hypothyroidism (p = 0.000). Studies done by Haddow JE et al7, Glinoer D et al19, Chen S et al 20, have increased need for NICU admissions among babies born to overt and subclinical hypothyroid mothers. Study by Sreelatha et al shows 14.6% had babies who had NICU admission.

V. Conclusions

Thyroid testing is a must at first booking, ideally prenatally to prevent miscarriages. As fetus needs thyroxine for brain development, growth, and lung maturation, adequate replacement therapy should be done to keep TSH with in trimester specific reference ranges. Early and effective treatment of thyroid disorders ensures safe pregnancy with minimal maternal and fetal complication.

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