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RESEARCH ARTICLE
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''STUDY OF PREVALENCE OF HYPOTHYROIDISM IN PREGNANT WOMEN'S''

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Abstract

Introduction- Thyroid dysfunction is a common disorder in pregnancy which affects both maternal and fetal outcomes. There are very less and limited data on prevalence of hypothyroidism during pregnancy from India because no such big study done till now. this study done to define cut off value of serum TSH level in Indian pregnant women as hypothyroid and maternal and fetal outcomes. Aim of study is ''Study of prevalence of hypothyroidism and adverse foeto-maternal outcome Indian pregnant women's''

Material and Methods - This is a prospective and retrospective cohort study conducted in a period of 1.5 years between September 2021 to April 2023, in the department of Obstetrics & Gynecology GMC Shahdol in 1000 pregnant women's who comes in antenatal checkup in opd. All healthy pregnant women with singleton pregnancy willing to participate in the study were enrolled. Women which have multiple pregnancy, known chronic medical disorder like diabetes, hypertension, any autoimmune disorder with hyperthyroidism or known hypothyroidism, bad obstetric history with a known cause are excluded from study.

However, there are few limitations of this study. We have not assessed trimester specific ranges. Follow up beyond newborn period was not possible because after discharge most infants either did not come for follow up or they were seen in pediatric clinic. We did not carry out thyroid examination using ultrasound, and we have not evaluated other causes of hypothyroidism in these women.

All pregnant women underwent ELISA TSH assay. Women with serum TSH >6.2mIU/L underwent Free Thyroxin (FT4) estimation and labelled as overt hypothyroid (OH) (group I) or subclinical hypothyroid (SCH) (group II). Women with serum TSH between 3-6.2mIU/L & 0.4-3mIU/L were labelled as group III & control. Foeto-maternal outcomes were compared between group I, II, III & controls

Result - The prevalence of SCH & OH was 6.4% and 3.8%. Pre-eclampsia, gestational DM & IUFD in group I and foetal distress in group II developed in significantly higher number of women (p=0.009,

p=0.002, p=0.002 & p=0.004 respectively) Foeto-maternal variables assessed in group III none was significantly different from control group.
Conclusion –. There is a high prevalence of hypothyroidism and adverse foeto-maternal outcome is more commonly associated with OH as compared to SCH. TSH 3-6.2mIU/L may be taken as normal during pregnancy in the Indian population. We recommend a higher cut off for serum TSH to diagnose hypothyroidism ie >6.2mIU/L in Indian pregnant women. The strong point of this study is that we have included large number of subjects from India. From this study we know the level of thyroid cut off level in Indian pregnant women's which can be used for diagnosis and treatment of this disorder.

Keywords – Hypothyroidism, pregnant women

INTRODUCTION

Thyroid disorder is a common in pregnancy and affects both maternal and fetal outcomes. There are limited data on prevalence of hypothyroidism during pregnancy from India.[1] The overall prevalence of hypothyroidism varies from 0.3-11.1% with subclinical hypothyroidism (SCH) being commoner than overt hypothyroidism. [2-14] due to their nonspecific symptoms and hypermetabolic state of pregnancy thyroid disorders are often overlooked in pregnancy most of the time. Serum TSH values of 4.0-6.0µIU/ml were considered normal in the past recent opinions suggest that first trimester values >2.5 µIU/ml and second and third trimester values >3µIU/ml are outside the normal range. [3,13,15,16]
Maternal hypothyroidism has been associated with adverse pregnancy complications as well as detrimental effects upon fetal neurocognitive development. Specific maternal adverse outcome includes anemia, abortion, preterm labour, gestational hypertension, preeclampsia and placental abruption. [4,13,16,1718,19] Fetal complications include prematurity, intrauterine foetal growth restriction, intrapartum foetal distress, foetal demise. [4,13,3,18,20,21]
Hence the laboratory measurement of thyroid dysfunction is very important role in the assessment of maternal thyroid health. The main stay of thyroid function evaluation is serum thyroxin stimulating hormone (TSH) assessment.[15] the thyroid dysfunction leads to physiological changes in pregnancy.
Keeping all these points in view this study was planned to analyze the foeto-maternal outcome in hypothyroid women with serum TSH >6.2mIU/L and in women having TSH between 3.0-6.2mIU/L, to establish a lower cut off value for serum TSH.
Aim- This is a prospective and retrospective cohort study conducted in a period of 1.5 years between September 2021 to April 2023, in the department of Obstetrics & Gynecology GMC Shahdol in 1000 pregnant women's who comes in antenatal checkup in opd. Aim of study is ''Study of prevalence of hypothyroidism and adverse foeto-maternal outcome Indian pregnant women's''.

MATERIAL AND METHODS

This is a prospective and retrospective cohort study conducted in a period of 1.5 years between September 2021 to April 2023, in the department of Obstetrics & Gynecology GMC Shahdol, in 1000 pregnant women attending the antenatal OPD were recruited for the study.
All healthy pregnant women with singleton pregnancy willing to participate in the study were enrolled; women if they had multiple pregnancy, known chronic medical disorder like diabetes, hypertension, any autoimmune disorder with hyperthyroidism or known hypothyroidism, bad obstetric history with a known cause, were excluded.
A detailed history & examination was performed, clinical features of hypothyroidism, past & family history of known thyroid dysfunction was noted. Serum samples were collected in plain vial for TSH estimation. The normal range for TSH is 0.4-6.2mIU/L for this laboratory. Women with serum TSH >6.2mIU/L labeled as hypothyroid according to laboratory reference range for TSH. Women labeled as hypothyroid were referred to endocrinology clinic for simultaneous treatment and follow up.

Maternal variables assessed were=

-anaemia
-spontaneous abortion

-gestational hypertension (GHTN)
-pre-eclampsia (PE)
-gestational diabetes mellitus (GDM)
-placental abruption
-mode of delivery

Foetal variables assessed were=
-prematurity
-intrauterine growth restriction (IUGR)
-intrauterine foetal demise (IUFD)
-foetal distress (FD)
-low APGAR – APGAR is ≤7 at 5minutes,
-neonatal intensive care unit admission (NICU)
-neonatal hypothyroidism – serum TSH level >20mU/L after 72 hours of birth.

Foeto-maternal outcomes were compared between group I, II, III and controls. Data was analyzed using Pearson Chi square test. The significance level was set at $p<0.05$. Statistical analysis was performed with SPSS 12.0 for window

RESULTS

Table 1: Demographic profile of Group III and Control

AGE (YEARS)	GROUP III (n=66)		Control (n=66)	
	Number	Percent (%)	Number	Percent (%)
≤20	6	9.09	6	9.09
21-25	44	66.66	44	66.66
26-30	13	19.69	13	19.69
31-35	3	4.54	3	4.54
PARITY				
Primigravidae	34	51.51	34	51.51
Multigravidae	32	48.48	32	48.48
EDUCATION				
Illiterate	33	50.00	32	48.48
Primary	15	22.72	17	25.75
Middle	14	21.21	12	18.18
Graduate	4	6.06	5	7.57
SOCIO-ECONOMIC STATUS				
Lower	4	6.06	8	12.12
Upper lower	31	46.96	33	50.00
Lower middle	18	27.27	16	24.24
Upper middle	9	13.63	5	7.57
Upper	4	6.06	4	6.06
OCCUPATION				
House wife	56	84.84	57	86.36
Self employed	2	3.03	3	4.54
Professional	8	12.12	6	9.09

Table 2: Comparison of maternal variables in OH, SCH (group I&II) &control

Maternal Variables	Overt Hypothyroid(I) (n= 21)		Euthyroid (n= 69)		*p* value	Subclinical Hypothyroid (grpII)(n= 48)		Euthyroid (n= 69)		*p* value
	number %		number %			number%		number%		
Anemia	17	80.95	49	71.01	0.367	35	72.91	49	71.01	0.822
Abortion	1	4.76	1	1.44	0.367	0	0	1	1.44	0.402
GHTN	2	9.52	2	2.89	0.197	3	6.25	2	2.89	0.378
PE	4	19.04	2	2.89	0.009	4	8.33	2	2.89	0.190
GDM	4	19.04	1	1.44	0.002	3	6.25	1	1.44	0.160
Placental abruption	0	0	0	0	-	0	0	0	0	-

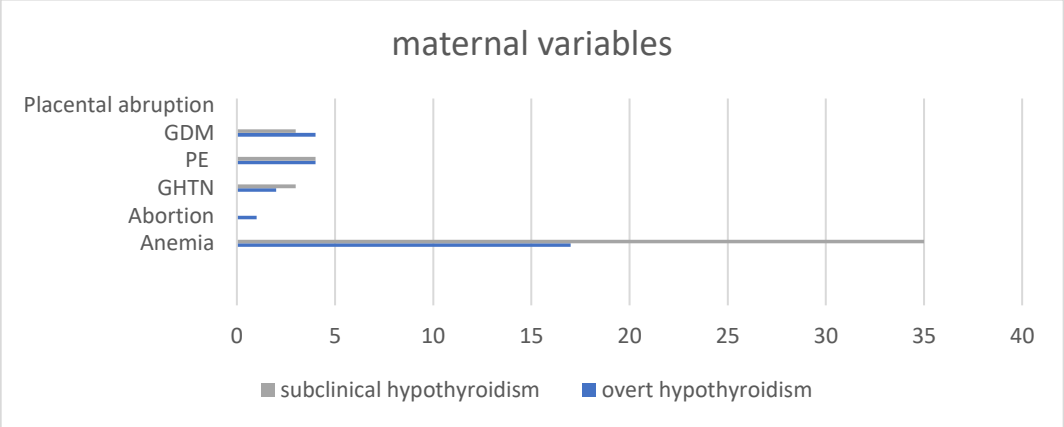

Table 2 illustrates the maternal variables assessed in group I & II. PE, GDM IUFD developed in significantly higher number of women in OH group as compared to controls (p=0.009, p=0.002, p=0.002). FD was observed in significantly higher number of women in SCH as compared to control (p=0.004), illustrated in table 3 &4.

Table 3: Comparison of foetal variables in OH, SCH (group I&II) &control

Foetal Variables	Overt Hypothyroid (groupI) (n= 21)		Euthyroid (n= 69)		*P* value	Subclinical Hypothyroid (group II) (n= 48)		Euthyroid (n= 69)		*P* value
	number%		number %			number%		number %		
PTB	1	4.76	4	5.79	0.203	3	6.25	4	5.79	0.919
IUGR	3	14.28	6	8.69	0.186	6	12.50	6	8.69	0.505
IUFD	4	19.04	1	1.44	0.002	1	2.08	1	1.44	0.795
Foetal Distress	3	14.28	6	8.69	0.455	14	29.16	6	8.69	0.004
Low APGAR at 5minute	1	4.76	4	5.79	0.856	5	10.41	4	5.79	0.356
NICU Admission	4	19.04	4	5.79	0.186	7	14.58	4	5.79	0.391
Neonatal hypothyroidism	0	0	0	0	-	0	0	0	0	-

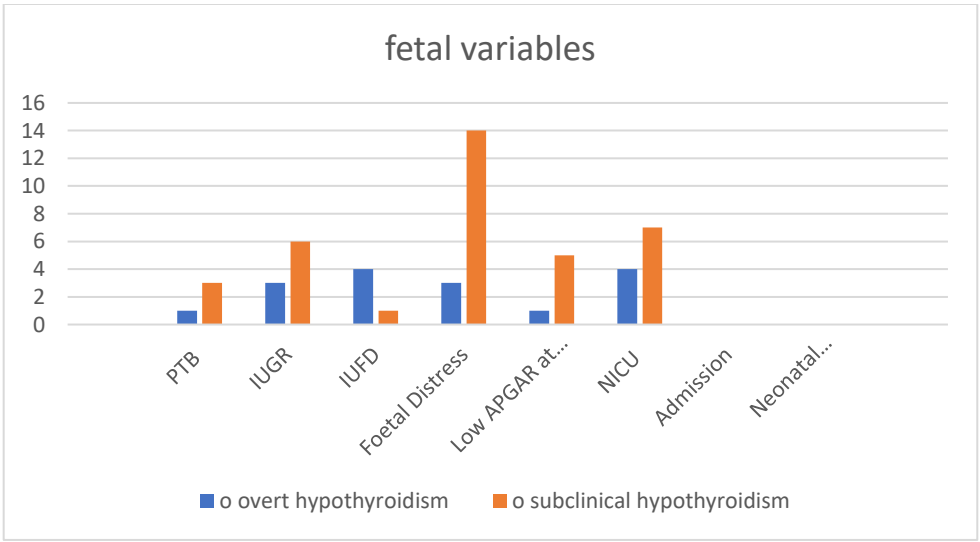

Table 4: Comparison of maternal variables in group III and control

Maternal Variables	**Group III (n=66)**		**Control (n=66)**		***p* value**
	number	**percent (%)**	**number**	**percent (%)**	
Anemia	48	72.72	48	72.72	1
Spontaneous Abortion	1	1.51	1	1.51	1
Hypertensive Disorders					
GHTN	0	0	2	3.03	0.154
Preeclampsia	2	3.03	1	1.51	0.559
GDM	4	6.06	1	1.51	0.171
Placental Abruption	0	0	0	0	

Table 5: Distribution of women according to mode of delivery

Mode Of Delivery	**Group III (n=65)** *		**Control (n=65)** *		***p* value**
	number	**Percent (%)**	**number**	**Percent (%)**	
Vaginal delivery	56	86.15	59	90.76	0.310
LSCS For FD	4	6.15	4	6.15	1
LSCS For Other causes	5	7.69	2	3.07	0.244

Majority of women in group I &II delivered vaginally. None other maternal or foetal variable compared showed significant difference. Table 4 and 5 demonstrates maternal and foetal variables assessed in group III and control. PE, GDM (p=0.559, p=0.171) and other maternal variables assessed none was significantly different from control group. Among foetal variables assessed IUGR, IUFD (p=0.545 p=0.154), and none other foetal parameter assessed was significantly different from control group. Equal number of women in both the groups had LSCS for foetal distress.

Table 6: Comparison of foetal variables in group III and Control

Foetal Variables	**Group III (n=66)**		**Control (n=66)**		***p* value**
	number (%)	**percent**	**number**	**Percent (%)**	
Preterm Birth	2	3.03	1	1.51	0.559
IUGR	7	10.60	5	7.57	0.545
IUFD	2	3.03	0	0	0.154
Foetal Distress	10	15.15	8	12.12	0.457
Low APGAR at 5 Minute	4	6.06	1	1.51	0.171
NICU Admission	5	7.57	2	3.03	0.300
Neonatal Hypothyroidism	0	0	0	0	-

DISCUSSION

The overall prevalence of hypothyroidism in our study was 10.2%, with SCH and OH being present in 6.4% & 3.8% women respectively. This value is similar to, an Indian study by Sahu et al who reported a prevalence of SCH and OH as 6.47% & 4.38% respectively.[13] these both studies done in tertiary health center.

These results are higher than developing countries, like USA, UK. Studies from USA have reported the overall incidence of hypothyroidism between 2.2%- 2.5% with an incidence of SCH and OH ranging from 2.2%-2.3% and 0.2%-0.3% respectively. [2,3,4]

Prevalence of both SCH & OH is higher in iodine deficiency regions in India.[22] The USA, UK and Finland are a relatively iodine sufficient countries; there is also have adequate iodine supplementation and even pregnant population has sufficient iodine intake. [6,7,22]

Studies conducted in the past, showed that by using the classical non-pregnant reference range, one might misdiagnose as "normal' those women who already have a slight TSH elevation.[15] ATA

Guidelines recommend that TSH upper cut off value for pregnant women & for women on L-thyroxin therapy should be <2.5IU/L in first trimester and <3.0IU/L in second and third trimester.[22]

Although several studies are available from different regions of the world it is essential to develop norms for Indian population. No difference was observed in the demographic profile of group III and control group.

Amongst all the maternal & foetal variables analyzed in this group, none were significantly different from the control group. These results indicate that women with TSH levels between 3-6.2mIU/L are at no added risk of adverse foeto-maternal outcome as compared to women with TSH <3mIU/L, hence no extra maternal & foetal monitoring is required for this group of women. Studies from countries like USA, China and Switzerland have established that serum TSH values during pregnancy are lower than the nonpregnant reference range, they have also determined trimester specific reference ranges for serum TSH during pregnancy.[28,29,30] The ATA recommends that if trimester specific reference ranges are not available, the upper cut off for serum TSH in pregnancy should be taken as 2.5mIU/L in the first trimester and 3.0mIU/L in second and third trimester.[22] The group III was designed to find out maternal and foetal outcome, by applying the lower serum TSH threshold in the Indian population; however, no statistically significant difference in maternal and foetal outcome was observed in this group as compared with controls.

The findings of our study are, however, consistent with the observations by Marwaha et al, in which the upper cut off for trimester specific serum TSH values in the Indian population were found to be higher i.e 5.0mIU/L, 5.78mIU/L and 5.70mIU/L in the first second and third trimester respectively.[11] The present study supports the observations of Marwaha et al and suggests that the serum TSH values in pregnant Indian women are higher than their counterparts in other countries due to ethnic variations, different environmental conditions and more so after two decades of salt iodization programme.[25,26,27] However, further studies are required to accurately define the normal range of serum TSH during pregnancy and to analyze the implications of serum TSH levels on pregnancy outcome, in a range that had previously been considered normal. Hence serum TSH (0.4-6.2mIU/L) in the nonpregnant range may be taken as normal during pregnancy in the Indian population, till we have population based Indian studies including larger cohorts, to establish trimester specific ranges in pregnant women.

In an Italian study, Negro et al compared the foeto-maternal outcome in women with serum TSH levels <2.5mIU/L and 2.5-5.0mIU/L, during the first trimester in TPO-Ab negative women. The study found a significant difference in the spontaneous pregnancy loss observed in the two groups (3.6% vs 6.1% respectively, p= <0.006). The study concluded that the increased rates of spontaneous foetal loss in women with serum TSH between 2.5-5.0mIU/L, provides strong support to redefine the normal serum TSH levels, especially in the first trimester.[16] The results of the present study are different from these observations. However, the sample size of our study was much smaller than that of Negro et al (66 vs 3481); besides, most women were enrolled during the second trimester as compared to 100% enrolment in the first trimester in the study by Negro et al.

We found that, untreated or uncontrolled overt hypothyroidism during pregnancy may increase the incidence of maternal anemia, preeclampsia, GDM, spontaneous abortion, LBW, fetal death or still birth. [13,18,31] In this study also the incidence of preeclampsia (p=0.009), GDM (p=0.002) was significantly high in overt hypothyroid group. In the past studies it has been shown that these women have higher incidence of PTB, IUGR, abruption, perinatal and neonatal morbidity and mortality. [19,32,33] Intrauterine foetal demise occurred in significantly higher number of women in OH group (p=0.002). FD was observed in significantly higher number of women in SCH (p=0.004). The overall rate of LSCS for foetal distress was not statistically different from controls.

The strong point of this study is that we have included large number of subjects from India. However, there are few limitations of this study. We have not assessed trimester specific ranges. Follow up

beyond newborn period was not possible because after discharge most infants either did not come for follow up or they were seen in pediatric clinic. We did not carry out thyroid examination using ultrasound, and we have not evaluated other causes of hypothyroidism in these women.

CONCLUSION

Based on the results of this study we conclude that Indian populations have high prevalence of hypothyroidism (10.2%), majority being subclinical (6.4%) & OH being 3.8% in Indian pregnant women. OH, is more commonly associated with adverse foeto-maternal outcome with respect to SCH. Serum TSH in the nonpregnant range may be taken as normal during pregnancy in the Indian population, till we have population based Indian studies including larger cohorts, to establish trimester specific ranges in pregnant women. We recommend a higher cut off for serum TSH to diagnose hypothyroidism ie >6.2mIU/L in Indian pregnant women and universal screening of hypothyroidism in our country to reduce the incidence of adverse foeto-maternal outcome.

From this study we know the level of thyroid cut off level in Indian pregnant women's which can be used for diagnosis and treatment of this disorder.

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