PREVALENCE OF OVERT AND SUBCLINICAL HYPOTHYROIDISM AMONG INDIAN PREGNANT WOMEN AND ITS EFFECT ON FOETOMATERNAL OUTCOME

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ABSTRACT

BACKGROUND

Thyroid disorders are amongst the commonest endocrinological disorders encountered in pregnancy. It is now well established that not only overt (OH), but Subclinical Hypothyroidism (SCH) also has adverse effects on maternal and foetal outcomes. Most of the studies are from the western population and only a few studies have analysed pregnancy outcome in hypothyroid Indian pregnant women. Presently, there is a paucity of Indian data on the prevalence and effect of hypothyroidism in pregnancy. Keeping all these things in mind, present study was aimed to find prevalence of hypothyroidism in pregnancy and its effect on foetomaternal outcome in Indian pregnant women studying a large population.

SETTINGS AND DESIGN

This was a cross-sectional study conducted in the Department of Obstetrics and Gynaecology, VMMC and Safdarjung Hospital, Delhi, in collaboration with the Departments of Endocrinology, Laboratory Medicine and Paediatrics.

MATERIAL AND METHODS

All women attending antenatal clinic between October 2010 and April 2011, underwent thyroid screening using Thyroid Stimulating Hormone (TSH) assay. Women with hypothyroidism were grouped into OH and SCH on the basis of Free T4 estimation. Pregnancy outcomes of these women were compared with pregnant women with normal TSH values.

STATISTICAL ANALYSIS USED

Data was analysed using Pearson Chi square test. Statistical analysis was performed with SPSS 12.0 for windows.

RESULTS

Overall prevalence of hypothyroidism was found to be 10.2% with SCH (6.4%) being commoner than OH (3.8%), 33 hypothyroid women excluded who were already on treatment. Out of 69 remaining hypothyroid women, 48 had SCH (69.56%) and 21 had OH (30.43%) and were categorised as group A1 and A2 successively. Preeclampsia (PE), Gestational Diabetes Mellitus (GDM) and Intrauterine Foetal Demise (IUFD) developed in significantly higher number of women in OH group as compared to controls (p=0.009, p=0.002, p=0.002). Anaemia, placental abruption, mode of delivery, prematurity, intrauterine growth restriction, foetal distress, neonatal intensive care unit admissions were comparable between the two groups. Amongst all foetomaternal variables assessed in SCH and control group, none was significantly different.

CONCLUSIONS

Our study shows a high prevalence of hypothyroidism, especially overt and subclinical hypothyroidism among Indian pregnant women with associated adverse perinatal outcome. There was no significant association between SCH pregnancy and adverse foetomaternal outcome; however, in overtly hypothyroid pregnant women the incidence of PE, GDM and IUFD was significantly higher as compared to euthyroid controls.

KEYWORDS

OH, SCH, TSH.

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INTRODUCTION

Thyroid disorders are amongst the commonest endocrinological disorders encountered in pregnancy.[1] The overall prevalence of hypothyroidism varies from 0.3-11.1% with Subclinical Hypothyroidism (SCH) being commoner than Overt Hypothyroidism (OH).[2-14]

Thyroid disorders are often overlooked in pregnancy because of their non-specific symptoms and the hyper-metabolic state of pregnancy.

Hence, the laboratory measurements of thyroid function play an important role in the assessment of maternal thyroid health.

The mainstay of thyroid function evaluation is serum Thyroxine Stimulating Hormone (TSH) assessment.[15]

Optimal maternal thyroid function during pregnancy is important for both the mother and the foetus. Maternal hypothyroidism has been associated with adverse pregnancy complications as well as detrimental effects upon foetal neurocognitive development. This is especially true during the first trimester, when the developing foetus is completely dependent on the mother for thyroid hormone that are critical for its growth and development. Specific adverse maternal outcomes include anaemia, abortion, preterm labour, gestational hypertension, preeclampsia and placental abruption.[4,13,16,17,18] Foetal complications include prematurity, Intrauterine Growth Restriction (IUGR), Intrapartum Foetal Distress (FD) and Intrauterine Foetal Demise (IUFD).[4,13,3,19,20,21] These complications are more frequent with OH than with SCH and adequate thyroxine treatment reduces the risk of poor obstetrical outcome.[15]

Presently, there is a paucity of Indian data on the prevalence and effect of hypothyroidism in pregnancy.[22] Most of the studies are from the western population and only a few studies have analysed pregnancy outcome in hypothyroid Indian pregnant women.[9,10,13,14]

Keeping all these points in view, this study was planned to determine the prevalence of hypothyroidism in pregnancy using a large population to study with TSH reference range (0.4-6.2 mIU/L) and to study the foetomaternal outcome in pregnant hypothyroid women with OH and SCH.

MATERIAL AND METHODS

This was a cross-sectional study conducted in the Department of Obstetrics and Gynaecology, VMMC and Safdarjung Hospital from October 2010 to April 2011, in collaboration with the Departments of Endocrinology, Laboratory Medicine and Paediatrics after taking clearance from the Ethical Committee of the hospital.

A total of 1000 pregnant women attending the antenatal OPD were consequently recruited for the study. Estimation of prevalence of hypothyroidism was based on serum TSH levels >6.2 mIU/L or evidence of pre-existing hypothyroidism. Out of the 1000 women, all healthy pregnant women with singleton pregnancy were included with informed written consent and all women with known chronic medical disorders like diabetes, hypertension, any autoimmune disorder, hyperthyroidism or known hypothyroidism on treatment, bad obstetric history with a known cause or with multiple pregnancy were excluded from the study. A detailed history and examination was performed with special regards to features suggestive of hypothyroidism, past and family history of known thyroid dysfunction was noted.

Serum samples were collected in plain vial for TSH estimation. TSH was measured by ELISA (Enzyme Linked Immunosorbent assay) technique from the central laboratory. The normal range for TSH is 0.3–6.2 mIU/L for this laboratory. Women with TSH >6.2 mIU/L were considered hypothyroid and underwent Free Thyroxin 4 (FT4) estimation to label them as OH (low FT4) and SCH (normal FT4). FT4 Reference Range of the laboratory was 0.76-2.24 ng/dL. Complete profile of thyroid hormone and TPO antibody estimation were not carried out in all pregnant women, for cost effectiveness in a low resource setting.

All the women with serum TSH >6.2 µIU/mL were referred to endocrinologist for a simultaneous treatment and follow-up and followed till delivery as per the routine hospital protocol. Serum TSH estimation was done in new-borns, 72 hours after birth to evaluate their thyroid function.

Maternal Variables Assessed were anaemia (Haemoglobin <11 gram percent), spontaneous Abortion (Spontaneous pregnancy loss prior to 20 weeks' gestation or with a foetus born weighing less than 500 gm, Gestational Hypertension [(GHTN) persistently elevated blood pressure of 140/90 mmHg or greater for the first time after mid-pregnancy without proteinuria, Pre-eclampsia [(PE) persistently elevated blood pressure of 140/90 mmHg or greater for the first time after mid-pregnancy with proteinuria; proteinuria is defined as 24-hour urinary protein excretion exceeding 300 mg], Gestational Diabetes Mellitus [(GDM) carbohydrate intolerance of variable severity with onset or first recognition during pregnancy], placental abruption (Premature separation of a normally situated placenta) mode of delivery Vaginal Delivery (VD)/Lower Segment Caesarean Section (LSCS) for foetal distress and for other causes.

Measured foetal outcomes included prematurity (Delivery before 37 completed weeks), IUGR (Birth weight less than tenth percentile for gestational age), IUFD (foetal death occurring after 20 weeks of pregnancy or/with foetal weight >500 grams), FD (non-reassuring foetal heart rate pattern or thick meconium stained liquor), low APGAR that is (i.e.) ≤7 at 5 minutes, neonatal Intensive Care Unit (NICU) admission, neonatal hypothyroidism serum TSH level >20 mU/L after 72 hours of birth.

Statistical Analysis

On the basis of serum TSH level, the women were categorized as group A with serum TSH level >6.2 mIU/L (Hypothyroid women). On the basis of FT4 level the women in group A were further divided into SCH (Group A1) and OH (Group A2). Equal number of age and parity matched controls were taken for group A with serum TSH level 0.4 - 6.2 mIU/L and labelled as Group B. Foetomaternal outcomes compared between group A and B and A1, A2 and B. Data was analysed using Pearson Chi square test. The significance level was set at $p<0.05$. Statistical analysis was performed with SPSS 12.0 for windows.

RESULTS

One thousand pregnant women attending the antenatal OPD were enrolled to determine the prevalence of hypothyroidism on the basis of serum TSH estimation. A total of 102 women had TSH >6.2 µIU/L, giving a prevalence of hypothyroidism as 10.2%. On further division with FT4 estimation, the prevalence of OH was 3.8% and that of SCH was 6.4%.

After determining the prevalence, 33 hypothyroid women who were already on treatment with Levothyroxine therapy were excluded from the study. The remaining 69 women with TSH >6.2 mIU/L were grouped in study Group A. On further division of group A with FT4 level, 48 women were categorised as group A1 with normal FT4 (SCH) and 21 women were categorised as group A2 with low FT4 (OH).

Age (Years)	Group A (n=69)		Group B (n=69)	
	Number	Percent (%)	Number	Percent (%)
≤20	5	7.24	5	7.24
21-25	29	42.02	28	40.57
26-30	24	34.78	25	36.23
31-35	11	15.94	11	15.94
Parity				
Primigravida	23	33.33	23	33.33
Multigravida	46	66.66	46	66.66
Education				
Illiterate	36	52.17	37	53.62
Primary	17	24.63	17	24.63
Middle	13	18.84	11	15.94
Graduate	3	4.34	4	5.79
Socio-economic status				
Lower	6	8.69	6	8.69
Upper Lower	37	53.62	41	59.42
Lower Middle	17	24.63	15	21.73
Upper Middle	6	8.69	4	5.79
Upper	3	4.34	3	4.34
Occupation				
Housewife	55	79.71	57	82.60
Self Employed	6	8.69	5	7.24
Professional	8	11.59	7	10.14

Table 1: Demographic Profile of Group A and B

- The mean age of the women in group A was 25.96±3.8 years and B was 26.17±3.9 years.
- Majority of women in group A and B were illiterate, belonged to upper lower class and were housewives respectively.

BMI kg/m²	GROUP A (n=69)		GROUP B (n=69)	
	Number	Percent (%)	Number	Percent (%)
<18.5	0		0	
18.5-24.9	35	50.72	34	49.27
25-29.9	30	43.47	31	44.92
≥30	4	5.79	4	5.79

Table 2: Distribution of Women According to BMI in Group A & B

Majority (50.72%) of the women in group A and most (49.27%) of the women in group B had normal BMI.

Maternal Variables	Group A (n=69)		Group B (n=69)		P value
	Number	Percent (%)	Number	Percent (%)	
Anaemia	52	75.36	49	71.01	0.564
Spontaneous Abortion	1	1.44	1	1.44	1
Hypertensive Disorder					
GHTN	5	7.24	2	2.89	0.245
PE	8	11.59	2	2.89	0.049
GDM	7	10.14	1	1.44	0.029
Placental Abruption	0	0	0	0	-

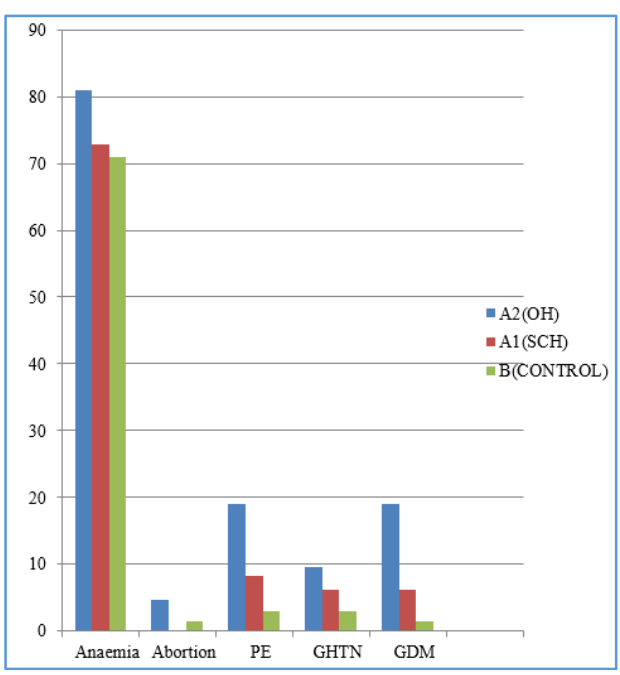
Table 3: Comparison of Maternal Variables in Group A and B

*n=68 as one women aborted in each group.

Mode of Delivery	Group A (n=68)*		Group B (n=68*)		p value
	Number	Number (%)	Number	Number (%)	
Vaginal delivery	53	77.94	56	82.35	0.541
LSCS For FD	9	13.23	4	5.88	0.145
LSCS for Other causes	6	8.82	8	11.76	0.573

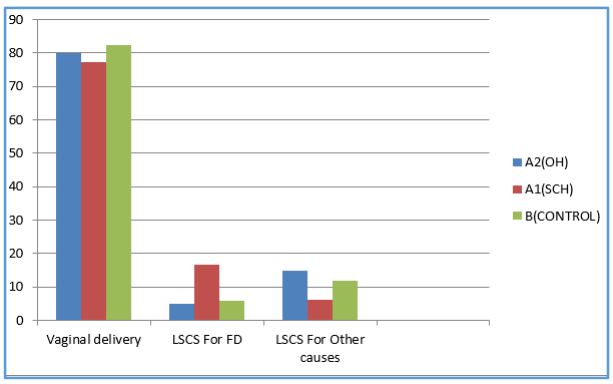
Table 4: Distribution of Women According to Mode of Delivery in Group A & B

- Preeclampsia and GDM developed in significantly higher number in group A as compared to group B respectively; (p=0.049, p=0.029), rest other parameters compared showed insignificant difference (Table 3).
- Most of the women in group A (77.94%) and B (82.35%) delivered vaginally and statistically insignificant difference was found on comparing LSCS for foetal distress between group A and B (Table 4).



Graph I: Comparison of Maternal Variables in OH, SCH and Control Group

- PE and GDM was developed in significantly higher number of OH women as compared to controls with p=0.009 and p=0.002 respectively, rest other parameters compared showed insignificant difference.



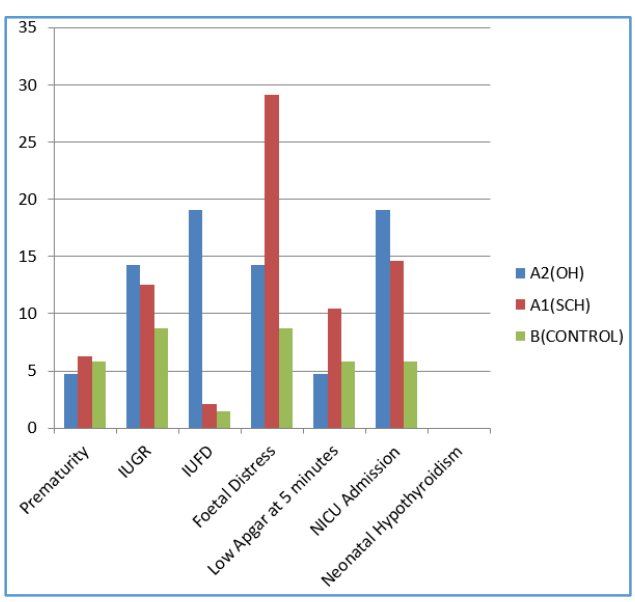
Graph II: Distribution of Women according to Mode of Delivery in OH, SCH and Control Group

- Majority of women in OH, SCH and euthyroid group delivered vaginally with p=0.424 and p=0.733 respectively and insignificant difference was found on comparing rate of LSCS performed for foetal distress.

Foetal Variables	Group A (n=69)		Group B (n=69)		p value
	Number		Percent (%)		
Prematurity	6	8.69	4	5.79	0.511
IUGR	10	14.49	6	8.69	0.288
IUFD	5	7.24	1	1.44	0.095
Foetal Distress	17	24.63	6	8.69	0.012
Low APGAR at 5 minute	6	8.69	4	5.79	0.511
NICU admission	11	15.94	4	5.79	0.191
Neonatal Hypothyroidism	0	0	0	0	-

Table 5: Comparison of Foetal Variables in Group A and B

- Foetal distress was significantly higher in group A as compared to group B, (p=0.012) other variables showed insignificant difference.



Graph III: Comparison of Foetal Variables in OH, SCH and Control Group

- OH (A2) group showed significantly higher IUFD (p=0.012) when compared with controls, the difference was insignificant between SCH (A1) and control (B), other compared parameters showed statistically insignificant difference.
- Amongst all the other foetal variables assessed between SCH, OH and control groups, none was statistically significant.
- None of the neonates in either of the groups had neonatal hypothyroidism.

DISCUSSION

Our study presents the first data on the prevalence and foetomaternal outcome in OH and SCH women covering a large population from north India. The predominant finding in this study is the high prevalence of hypothyroidism observed (10.2%) with SCH and OH being present in 6.4% and 3.8% women respectively. Our observations are similar to those of an Indian study by Sahu et al who reported a prevalence of SCH and OH as 6.47% and 4.38% respectively.[13]

Both these studies were conducted in tertiary care hospitals, which are important referral centres; hence, they get a large number of referral cases even from neighbouring states. The relevance of this finding is substantiated by the adverse perinatal outcome. Most of the studies on hypothyroidism among pregnant women are from our western counterpart, which showed a prevalence ranging from 0.23-3.9% for SCH and 0.3-1% for OH.[3-8] All these studies vary in their definition of hypothyroidism and sample size. Besides, there are differences in the iodine intake of the population screened. Few studies have been done among South Asian pregnant women reporting increased risk of thyroid dysfunction.[6] It was therefore important to conduct the present study, because the findings of other studies may not apply to an Indian population.

Prevalence of both SCH and OH is likely to be higher in iodine deficiency regions.[22,20,11] The United States of America, United Kingdom and Finland are relatively iodine sufficient countries; there is adequate iodine supplementation and even pregnant population has sufficient iodine intake.[6,7,22] On the other hand, the situation of Indian pregnant women is different. Although Marwaha et al have reported that India has become iodine sufficient after two decades of salt iodisation, there is no normative data for thyroid function for healthy pregnant women of this country.[11] In a review of nine studies on the assessment of iodine nutrition of pregnant women in India, Yadav et al, identified significant iodine deficiency among pregnant Indian women. According to the review, the household level of adequately iodised salt consumption in pregnant women ranged from 59.5% to 95%. However, even a 95% household level coverage of adequately iodised salt may not lead to iodine sufficiency in pregnant women.[23] This is because the current Salt Iodisation Guidelines (15 ppm of iodine at consumer level) is designed to deliver only 150 µg/L of iodine per day, whereas the dietary requirements of pregnant women are much greater (250 µg/day). The current available data in India shows that pregnant women in India are iodine deficient as per the World Health Organization/United Nations International Children's Emergency Fund criterion.[24] This is probably the reason for the high prevalence of hypothyroidism observed in the present study and by Sahu et al.

The group A and B were age and parity matched and there was no difference in other baseline demographic characteristics of women between the two groups. As seen in previous studies, untreated or uncontrolled overt hypothyroidism during pregnancy may increase the incidence of maternal anaemia, preeclampsia, spontaneous abortion, GDM, LBW, fetal death or still birth.[9,13,19,25] In this study also, the incidence of PE (P=0.009), GDM (0.002) and IUFD (P=0.012) was significantly higher in overt hypothyroid group. The association of PE with hypothyroidism could be due to abnormal thyroid hormones which lead to endothelial cell dysfunction, reduction in nitric oxide and impaired vasorelaxation.[26] The incidence of GHTN in the two groups was, however, comparable.

The present study did not observe any association of SCH with GDM. Similar results have been reported by Cleary Goldman et al, who did not find any association between GDM and SCH (3.0% in euthyroid, 2.6% and 1.7% in SCH in first and second trimester).[5] On the contrary, Casey et al have reported a higher incidence of GDM in SCH. The study linked the high incidence with increased maternal age and body weight, because in their study group women with SCH were older and heavier than control group. None of the women in either of the groups had placental abruption. Our results are similar to those of Mannisto et al who reported no association between hypothyroidism and abruptio placentae.[7] (0.5% in SCH Vs 0.5% in euthyroid). Cleary Goldman et al also did not find any association of SCH with abruptio placentae (First trimester 0.9% in both SCH and controls, in second trimester 0.8% in SCH and 0.9% in controls).[5] Sharma et al reported antepartum haemorrhage in 4.25% in control and 2.44% in hypothyroid women.[10] However, Casey et al have reported that incidence of abruption was three times higher in SCH (1.0%) group as compared to controls (0.3%) p=0.0264.

In group A2, only one woman had spontaneous abortion. She presented at 8 weeks with OH with very high serum TSH level (93.3 μIU/L) and aborted at 11 wks. despite initiation of L-thyroxine substitution therapy at 9 wks. Our results are similar to that of Cleary Goldman et al who found no significant association between SCH group and spontaneous abortion (0.6% in euthyroid, 0.4% and 0.9% in SCH in first and second trimester respectively.[5] In our study, most of the women were enrolled in the second trimester by which time most miscarriages would have already occurred. Hence, the rate of abortions may not have been accurately assessed in the present study.

The present study observed a significantly higher incidence of FD in group A women as compared to group B (p=0.012). This remain significant only with SCH group [A1] (p=0.004). FD as an indication for LSCS was also observed in a larger percentage of hypothyroid women (13.23%) as compared to controls (5.79%); however, the difference was not statistically significant. Because the mechanism of disease whereby thyroid hormone deficiency leads to preterm labour, placental abruption and other pregnancy complications is not known, we can only speculate about the association of FD with maternal hypothyroidism. One unifying hypothesis is that thyroid hormone is necessary for normal placental development. Specifically, there is evidence that preterm delivery and vascular diseases such as preeclampsia and placental abruption may be causally linked to faulty early placentation.[27,28]

Besides there may be hypoxic changes in placentae of hypothyroid women, which may be responsible for foetal distress seen frequently in hypothyroid pregnant.[10]

No significant association between maternal hypothyroidism and anaemia, prematurity, low APGAR, NICU admission and neonatal hypothyroidism was observed between group A, A1 and A2 with group B as seen in earlier studies.[5,7,13]

To accept the weaknesses of our study, we did only TSH test initially and then checked FT4 when the TSH was high. There is a possibility that this strategy would have missed patient with isolated hypothyroxinaemia (Low FT4 and normal TSH) and did not do TPO antibodies, so women who are antibody positive and euthyroid. 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 Paediatric Clinic. Further studies are required to establish trimester specific reference ranges for pregnant Indian women.

Our study shows a high prevalence of hypothyroidism, especially overt and subclinical hypothyroidism among Indian pregnant women with associated adverse perinatal outcome. Based on the results of the present study; we, therefore, suggest that all pregnant women should be screened with TSH at their first antenatal visit and L-thyroxine therapy should be initiated as early as possible, even in the pre-conceptional period wherever feasible and to be potentially aware of associated maternal and foetal complications. Antepartum surveillance for foetal wellbeing is required due to the high risk of intrauterine foetal demise. Intensive intrapartum foetal monitoring is mandatory to detect foetal distress at an early stage.

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