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**Research Article**

# PREVALENCE AND EFFECT OF SUBCLINICAL HYPOTHYROIDISM ON PREGNANCY OUTCOME-A STUDY IN EASTERN INDIA

**Debasmita Mandal*., Sanchita Roy., Rashmi Baid., Amitava Das and Subhankar Choudhary**

Deparment of Obst&Gyne, PGME & R, SSKM Hospital, 244 AJC Bose Road, Kolkata-700020, West Bengal, India

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**ABSTRACT**

**Background:** Pregnancy with subclinical hypothyroidism may have adverse outcome.
**Objectives:** Our aims are to find out the prevalence of SCH in pregnancy, to analyse the effect of SCH on pregnancy outcome and also to observe recent neonatal outcome.
**Results:** Prevalence of SCH was 4.07. Pregnancies with SCH were more likely to be complicated with pregnancy induced hypertension (26.67%), abruptio placentae (10%), oligohydramnios (16.67%) & IUGR (23.33%). In postpartum period 10% of women with SCH suffered with maternal sepsis & wound dehiscence, whereas subinvolution was seen in 6.67% cases. Neonates also suffered more with RDS (6.67%), neonatal jaundice (20%) and sepsis (13.33%). There was increased incidence of retro placental clots (10.00%) & calcification (13.33%) in women with SCH.
**Discussion:** Subclinical hypothyroidism in pregnancy may result in unfavorable obstetric outcome. Timely screening, therapeutic interventions and multidisciplinary approach will culminate into desired pregnancy outcome.



## INTRODUCTION

Hypothyroidism during pregnancy is deleterious to both mother and child, is almost a known fact[1]. But subclinical hypothyroidism may also have a profound effect on pregnancy. It is defined as an elevation of serum thyrotropin (TSH) above the normal reference limit with normal serum free thyroxin e(FT4) concentration with no specific symptoms or signs of thyroid dysfunction[2]. Production of thyroid hormones and iodine requirement each increases by approximately 50% during pregnancy[3]. It creates hypothyroidism in women with limited thyroidal reserve or iodine deficiency. That's why subclinical thyroid dysfunction probably are more prevalent and remain frequently unrecognized, untreated or undertreated.

During pregnancy, thyroid gland may enlarge by 10% in iodine sufficient countries and to greater extent in iodine poor places[4]. Overt maternal hypothyroidism is associated with fetal neurogical impairment and mental retardation as well as pregnancy complications that include preeclampsia, placental abruption, preterm birth, low birth weight and fetal death[5,6]. The effects of mild maternal deficiency with a normally functioning fetal thyroid gland are less clear. Screening for and treating subclinical hypothyroidism during pregnancy are subjects of ongoing debate and research. The prevalence of subclinical hypothyroidism in Indian women and its effect on pregnancy outcome is not exactly known as we do not have adequate published data. There is no study available indicating the prevalence of subclinical hypothyroidism in pregnancy in Eastern Indian population. Thus this study has been undertaken among pregnant women attending IPGME&R, government hospital of Kolkata, West Bengal, Eastern India to define the magnitude of problem and its effect on pregnancy outcome.

The objectives were-a) to find out prevalence of subclinical hypothyroidism in pregnant women, b) to find out the effect of subclinical hypothyroidism on obstetrics, c) to evaluate the neonatal outcome in women with subclinical hypothyroidism.

## MATERIAL S AND METHODS

This study was conducted in the Department of Obstetrics and Gynaecology, IPGME&R, SSKM Hospital, Kolkata in collaboration with Departments of Endocrinology and Neonatology.

This prospective cohort study of one year (1ST July 2011 to 30TH June 2012) was undertaken after approval from the Institutional Ethics Committee. The pregnant women were included from booked antenatal cases attending outpatient department and also from unbooked cases getting direct

*Corresponding author: **Debasmita Mandal***
*Deparment of Obst&Gyne, PGME & R, SSKM Hospital, 244 AJC Bose Road, Kolkata-700020, West Bengal, India*

admission to the ward with some antenatal complications who gave a written informed consent.

Seven hundred thirty seven cases of pregnant women with singleton live foetus at 36-38 weeks period of gestation were selected. Exclusion criteria were, women with already known thyroid disease, symptoms suggestive of thyroid dysfunction, multiple pregnancies and history of autoimmune disease & type-1 Diabetes Mellitus.

All patients were subjected to a detailed history and clinical examination using a predesigned proforma. Thyroid function studies were performed using chemiluminescent assays by Immulite 1000, Siemens for TSH and free thyroxine (FT4). The accepted range of TSH for euthyroid person was 0.3 to 3m IU/L. For pregnant women this cut off level was dropped to 2.5 m IU/ L. Subclinical hypothyroidism was defined according to the clinical features and an elevated TSH (TSH< 10m IU/ L) with normal T4. Maternal monitoring was done for development of complications like hypertension, placental abruption, preterm labour, fetal growth restriction, postpartum haemorrhage etc. Newborn thyroid values were also assessed after 48hrs of life by flurometric assay. Follow up of mother and newborn were done till discharge from hospital.

The data were entered in Excel sheet and percentage of various outcome measures were calculated using Statistica version 6 & GraphPad Prism version 5.

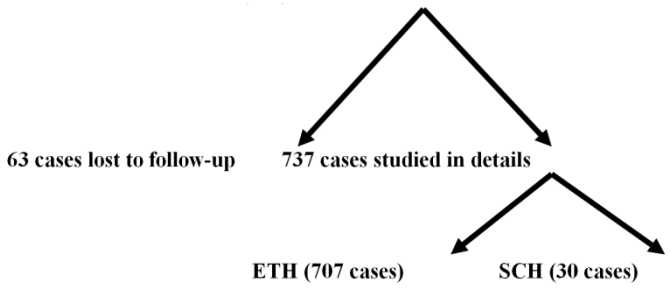
## RESULTS

Eight hundred antenatal patients were screened for thyroid function. Out of this 800 pregnant women, 63 cases were lost to follow-up and were excluded from statistical analysis.

Thirty antenatal mothers have been diagnosed to have subclinical hypothyroidism (SCH). Another 90 euthyroid (ETH) women have been selected as control matched to cases in age, parity and ethinicity. These cases were critically analyzed and compared in the light of different parameters

***Categorization of total enrolled Antenatal mothers***

**Total Antenatal mothers (800)**




***Statistically Analysed and Compared - 90 ETH AND 30 SCH CASES***

The prevalence of subclinical hypothyroidism was 4.07%. Majority women were in the age group 21-25 years. (51.11%). There was no correlation of prevalence of subclinical hypothyroidism with age. When both group women were analysed in terms of parity and body mass index, no statically significance result turned up (Table1).

**Table1** Distribution of various parameters among women with Subclinical hypothyroidism (SCH) and Euthyroidism (ETH)

| PARAMETERS | ETH | SCH | p value |
|---|---|---|---|
| Age | 24.3±3.33 | 24.2±3.11 | 0.885 |
| Residence | | | |
| Rural | 59(65.56%) | 23(76.67%) | 0.364 |
| Urban | 31(34.41%) | 7(23.33%) | |
| Parity | | | |
| Primi | 56(62.22%) | 16(53.33%) | 0.399 |
| Multi | 34(37.78%) | 14(46.67%) | |
| BMI | 22.77±2.31 | 22.92±2.18 | 0.636 |
| Hb% | 10.68±0.65 | 10.16±0.57 | 0.546 |

**Table 2** Comparison of pregnancy outcomes between pregnant women with Subclinical hypothyroidism (SCH) and Euthyroidism (ETH)-Fisher's exact test

| Pregnancy outcome | ETH n (%) (n=90) | SCH n(%) (n=30) | Odd's ratio | p-value |
|---|---|---|---|---|
| PIH* | 4(4.44) | 8(26.67) | 7.818(2.155-28.364) | 0.002 |
| Pre eclampsia | 3(3.33) | 4(13.33) | 4.462(0.937-21.234) | 0.065 |
| Eclampsia | 1(1.11) | 0(0) | 0.978(0.039-24.670 | 1.000 |
| Abruptio placentae | 1(1.11) | 3(10.00) | 9.889(0.987-99.063) | 0.048 |
| Oligohydramnios | 3(3.33) | 5(16.67) | 5.800(1.295-25.974) | 0.023 |
| *FGR | 6(6.67) | 7(23.33) | 4.261(1.304-13.926) | 0.018 |
| *IUFD | 1(1.11) | 0(0) | 0.978(0.039-24.670) | 1.000 |
| Onset of labor | | | 0.511(0.147-1.777) | 0.313 |
| a)Spontaneous | 47(82.46) | 12(70.59) | | |
| b)Gel induction | 10(17.54) | 5(29.41) | | |
| Mode of delivery | | | 1.023(0.447-2.234) | 1.000 |
| Vaginal delivery | 45(50.56) | 15(50) | | |
| *LSCS | 44(49.44) | 15(50) | | |

Pregnancy Induced Hypertension*, Foetal growth restriction *, Intrauterine Fetal Death*, Lower segment caesarean section*

Table 2 observed compared results of pregnancy outcomes in women with subclinical hypothyroidism and euthyroidism. The present study noticed pregnancy induced hypertension (PIH) **(**26.67% vs 4.44%; p<0.002**),** preeclampsia (13.33% vs 3.33%, p= 0.065), oligohydramnios (16.67% vs 3.33%; p=0.023) and foetal growth restriction (6.67% vs 23.33%; p= 0.018) were more associated with subclinical hypothyroidism than euthyroid pregnant women. But in terms of intrauterine foetal death and eclampsia the statistical analysis between two groups remained insignificant. Pregnancies in women with subclinical hypothyroidism were three times more likely to be complicated by placental abruption when compared with healthy pregnant women. (p-value0.048).

Postnatal events in women with subclinical hypothyroidism were compared with euthyroidism in table3.

**Table3** Comparison of postnatal events between pregnant women with Subclinical hypothyroidism (SCH) and Euthyroidism (ETH)-Fisher's exact test

| Postpartum events With findings | ETH n (%) (n=90) | SCH n (%) (n=30) | Odd's ratio | p-value |
|---|---|---|---|---|
| Postpartum Haemorrhage | 2(2.22) | 0(0.00) | 0.580(0.027-12.43) | 1.000 |
| Subinvolution | 1(1.11) | 2(6.67) | 6.357(0.555-72.81) | 0.154 |
| Maternal Sepsis | 0(0.00) | 3(10.00) | 23.036(1.153-460.160) | 0.014 |
| Wound dehiscence | 1(1.11) | 3(10.00) | 9.889(0.987-99.063) | 0.048 |
| Retroplacental clots | 1(1.11) | 3(10.00) | 9.889(0.987-99.063) | 0.048 |
| Calcification | 1(1.11) | 4(13.33) | 13.692(1.465-127.970) | 0.014 |

This study observed more incidences of subinvolution (6.67% vs 1.11%; p=0.154), maternal sepsis (10% vs 0%; p=0.014) and

wound dehiscence (10% vs 1.11%; p=0.048) with subclinical hypothyroidism. Although PPH was seen more in euthyroidism no previous study regarding observation of postnatal events in subclinical hypothyroidism is available. Women with SCH were observed to be associated more with retro placental clots and placental calcification.

Table 4 showed selected neonatal outcomes in women with subclinical hypothyroidism compared with euthyroidism. It has been observed that in the present series jaundice, sepsis and NICU admission are more associated with SCH than ETH pregnant women. No significant difference has been noted for respiratory distress syndrome in between two groups. There was not any significant difference in birth weight of baby in both the groups. None of the babies born had any congenital malformation.

**Table 4** Comparison of neonatal outcomes between pregnant women with Subclinical hypothyroidism (SCH) and Euthyroidism (ETH)-Fisher's exact test

| Neonatal outcome | ETH n (%) (n=90) | SCH n(%) (n=30) | Odd's ratio | p-value |
|---|---|---|---|---|
| Birth weight | | | | |
| a)1.7-2.4 | a)23(25.55) | 8(26.67) | | 0.226 |
| b)>2.4 | b)67(74.44) | 22(18.33) | | |
| *RDS | 0(0.00) | 2(6.67) | 15.877(0.740-340.720) | 0.061 |
| Jaundice | 2(2.22) | 6(20.00) | 11.000(2.085-58.035) | 0.003 |
| Neonatal Sepsis | 2(2.22) | 4(13.33) | 6.769(1.173-39.083) | 0.034 |
| *NICU admission | 3(3.33) | 7(23.33) | 8.826(2.115-36.837) | 0.003 |

Respiratory distress syndrome*, Neonatal Intensive Care Unit*.

## DISCUSSION

This study was aimed to evaluate the effect of subclinical hypothyroidism on pregnancy outcome. There are several important findings from this prospective analysis of 737 pregnant women who underwent screening for abnormal thyroid function at 36-38 weeks gestational age. First, the prevalence of subclinical hypothyroidism was 4.07%. Casey MB *et al* showed prevalence of 2-5% in pregnant women which corresponded with present study [7]. It concord virtually with all previous reports [8,9 ,10, 11]. Second, women with subclinical hypothyroidism had a significantly higher incidence of PIH, preeclampsia, oligohydramnios and foetal growth restriction.

A third observation was a significant three-fold increase in the incidence of placental abruption in women in the subclinical hypothyroid group compared with healthy controls, which corresponds to the study done by Casey MB *et al* [7]. Fourthly, postpartum complications like maternal sepsis, wound dehiscence and subinvolution, retroplacental clots and placental calcification were more associated with subclinical hypothyroidism. No previous study regarding observation of postnatal events and observation of placental features in subclinical hypothyroidism is available. A fifth finding was that the proportion of infants of mothers with subclinical hypothyroidism admitted to the neonatal intensive care unit as well as those who developed neonatal sepsis was significantly doubled when compared with infants of euthyroid women. Neonatal jaundice was also seen to be more associated with infants of mothers with subclinical hypothyroidism. The present study had no significant difference of birth weight of baby which corroborates with the study of Casey *et al* [7]. In this present study no congenital malformation was noted. This analysis did not show statistical significance between two groups regarding the onset of labour and mode of delivery. Here caesarean section were conducted with obstetric indications only. Per se SCH is not an indication of caesarean section.

Two debatable issues arise here whether identification and thyroid hormone supplementation of women with subclinical hypothyroidism would prevent or modify the outcome. Therapy beginning after 10 weeks of gestation would not eliminate any already established foetal neuro developmental impairment from hypothyroxinemia. Pop and colleagues have provided evidence that treatment may be ineffective only if given after this time [12]. Because the mechanism of disease whereby thyroid hormone deficiency leads to placental abruption, and other pregnancy complications is not known, we can only speculate about any salutary effects of thyroxine replacement. One unifying hypothesis is that thyroid hormone is necessary for normal placental development. Specifically, there is evidence that vascular diseases such as preeclampsia and placental abruption may be causally linked to faulty early placentation [13,14]. Although our findings may provide further incentive to screen for subclinical hypothyroidism in pregnancy, there are currently no randomized controlled treatment trials to substantiate such a policy.

This study concludes that there is a high prevalence of subclinical hypothyroidism in pregnant women in India. Hence there is a need for universal thyroid screening in pregnancy, especially in the first trimester when the foetal thyroid tissue is not functional. The role of routine screening becomes all the more relevant in these patients as they are asymptomatic and symptoms if any are ascribed to pregnancy itself. In a country like India where the pregnancy rate is very high because of sheer magnitude of the population and where majority of women seek antenatal care at government institutions, such simple screening procedures could have profound implications on the health of the nation. Although our findings may provide further incentive to screen for subclinical hypothyroidism in pregnancy, there are currently no randomized controlled treatment trials to substantiate such a policy.

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