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Original Research Article

Observational comparative study in pregnant females between normal thyroid profile and subclinical hypothyroidism in first trimester and its effect on pregnancy and fetomaternal outcome

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ABSTRACT

Background: Subclinical hypothyroidism (SH) by definition means there is increased in serum thyroid stimulating hormone (TSH) and normal free T4 and free T3. Normal range of serum TSH according to trimester is given below (as per American Thyroid Association and Endocrine Society Clinical Practice Guidelines recommendations): 1st trimester: 0.1 to 2.5 mIU/l; 2nd trimester: 0.2 to 3.0 mIU/l; 3rd trimester: 0.3 to 3.0 mIU/l. Numerous studies have demonstrated association of SH with adverse pregnancy related outcome while some studies found no association. This study was conducted to study about SH in pregnancy and its impact on fetomaternal outcomes.

Methods: This was a hospital based prospective case control study, conducted on 100 women taking routine antenatal care between year 2023 and 2024. The participants were divided into two groups - case: antenatal women in 1st trimester with SH, and control: antenatal women with 1st trimester with normal thyroid profile. These women were followed till their delivery and their maternal and neonatal outcomes were compared.

Results: Women with SH reported increased risk of complications (anaemia, preeclampsia, postdatism, oligohydramnios, more NICU admissions and low APGAR score).

Conclusions: Evaluation for altered thyroid profile in early pregnancy should be done routinely and timely intervention for treatment even for subclinical hypothyroidism to be done. It will lead to decrease in all complications and will improve the maternal and neonatal outcome.

Keywords: Subclinical hypothyroidism, Maternal outcome, Neonatal outcome

INTRODUCTION

The incidence of thyroid dysfunction is 2.3–3.8% of women in pregnancy. The subclinical hypothyroidism manifestations occur in 2.3% cases.^{1,2} Subclinical hypothyroidisms in pregnancy is defined as increased in serum thyroid stimulating hormone (TSH) and normal free T4 and free T3.

Normal range of serum TSH according to trimester is given below (as per American Thyroid Association and Endocrine Society Clinical Practice Guidelines recommendations) - 1st trimester: 0.1 to 2.5 mIU/l, 2nd

trimester: 0.2 to 3.0 mIU/l, and 3rd trimester: 0.3 to 3.0 mIU/l.

In 1999, interest was heightened by two studies indicating that undiagnosed maternal thyroid hypofunction may impair fetal neuropsychological development. In one study, Pop et al described 22 women with free T4 levels <10th percentile whose offspring were at higher risk for impaired psychomotor development. In the other study, Haddow et al retrospectively evaluated children born to 48 untreated women whose serum TSH values were >98th percentile. Some had diminished school performance, reading recognition, and intelligent quotient (IQ) scores.³

To further evaluate any adverse effects, Casey et al identified subclinical hypothyroidism in 2.3 percent of 17,298 women screened at Parkland Hospital before midpregnancy. These women had small but significantly higher incidences of preterm birth, placental abruption, and neonates admitted to the intensive care nursery compared with euthyroid women. In another study of 10,990 similar women, however, Cleary-Goldman et al did not find such associations.²

Other studies by Chen et al and Maraka et al subsequently confirmed a link between subclinical thyroid function and adverse outcomes. One included 24,883 women screened throughout pregnancy and showed an almost twofold greater risk of severe preeclampsia. In an analysis of the same cohort, a consistent relationship was shown between rising TSH levels and the risk for gestational diabetes. Finally, Nelson et al found an elevated risk for diabetes and stillbirth.

Lazarus et al reported the findings of the international multicenter controlled antenatal thyroid screening (CATS) study. This study evaluated prenatal thyroid screening and randomized treatment of both subclinical hypothyroidisms. They reported that offspring IQ scores at age 3 years were not superior in the treated pregnancies.

Despite these findings, the unanswered question concerned whether treatment of subclinical hypothyroidism would mitigate any or all of these reported adverse outcomes.

To address this, the maternal-fetal medicine units network screened more than 97,000 pregnant women for thyroid disorders and reported that 3.3 percent had subclinical hypothyroidism. These 677 women were randomly assigned to thyroxine replacement therapy or placebo. As reported by Casey et al, maternal adverse pregnancy outcomes or cognitive development in the offspring at 5 years did not differ between groups. Annual developmental testing scores and behavioral and attention-deficit hyperactivity disorder results also did not differ.

Because of earlier study findings, some professional organizations began to recommend routine prenatal screening and treatment of subclinical hypothyroidism. However, after CATS and MFMU network studies, more recent clinical practice guidelines from Endocrine Society, the American Thyroid Association and American Association of Clinical Endocrinologists now uniformly recommends screening only those which are at greater risk during pregnancy.

METHODS

This was a prospective case control study. This study was conducted in the Department of Obstetrics and Gynecology at Tertiary Care Institute of Central Gujarat between February 2023 and August 2024.

Study was conducted on 100 antenatal women of which 50 belonged to case group and 50 belonged to control group for comparison.

Case

Antenatal women in 1st trimester with sr. TSH >2.5 mIU/l and less than or equal to 5 mIU/l and normal free T3 and free T4 i.e. women with SH.

Control

Antenatal women with 1st trimester with normal sr. TSH (less than or equal to 2.5) and normal free T3 and free T4 ie euthyroid women.

Exclusion criteria

Antenatal women with k/c/o hypothyroidism with or without treatment, and antenatal women k/c/o hyperthyroidism with or without treatment were excluded.

All antenatal women in 1st trimester had undergone thyroid profile testing. Women with serum TSH 0.1 to 2.5 mIU/l and normal free T3 and T4 are grouped as euthyroid (controls). Women with serum TSH 2.5 to 5 mIU/l with normal free T3 and T4 were grouped as subclinical hypothyroidism (cases). 50 of the cases and 50 of the controls were selected for study purpose.

A detailed history was taken after noting the socio-demographic data which included age, socioeconomic status, education and occupation. History including chief complaints, weeks of pregnancy, past history, signs of thyroid disorders, menstrual history, obstetric history, past medical history, family history and personal history was taken.

Women are asked for routine antenatal visits in the OPD. During each visit, a thorough general physical examination with reference to pulse, BP, temperature, respiratory rate was followed by systemic examination and local thyroid examination. Per abdomen examination was done.

At the end obstetric outcomes, perinatal outcome and neonatal outcomes were observed and compared among two groups.

Data entry was done in Microsoft excel and analysis was done using a software Epi Info 7.

RESULTS

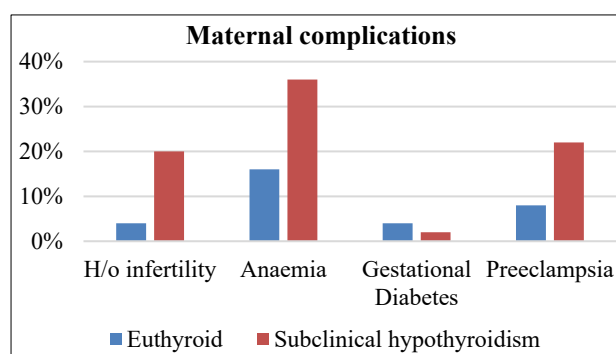
The mean age of women belonged to euthyroid group is 24.62 (SD: 4.02) which is comparable to women belonged to subclinical hypothyroidism which is 24.67 (SD: 4.5). The mean BMI is also similar in both the groups {24.2 (control) versus 24.6 (cases)}.

Table 1: Maternal characteristics.

Variables	Mean age	BMI (kg/m ²)
Euthyroid	24.62 (SD: 4.02)	24.2±4.0
Subclinical hypothyroidism	24.67 (SD: 4.5)	24.6±3.5

Table 2: Maternal complications.

Complications	Euthyroid (control) (%)	Subclinical hypothyroidism (cases) (%)
History of infertility	4	20
Anaemia	16	36
Gestational diabetes mellitus	4	2
Preeclampsia	8	22

**Figure 1: Comparison of maternal complication among two groups.**

18 (36%) of antenatal women with subclinical hypothyroidism had anaemia as compared to 8 (16%) of antenatal women with normal thyroid profile. The results were statistically significant (p value: 0.01).

In antenatal women with normal thyroid profile, 2 (4%) had history of infertility as compared to antenatal women with subclinical hypothyroidism, 10 (20%) had history of infertility. The differences were statistically significant (p value: 0.01).

Gestational diabetes was noted in 2 (4.0%) and 1 (2%) in euthyroid antenatal women and antenatal women with subclinical hypothyroidism respectively. This difference was not statistically significant (p=0.31).

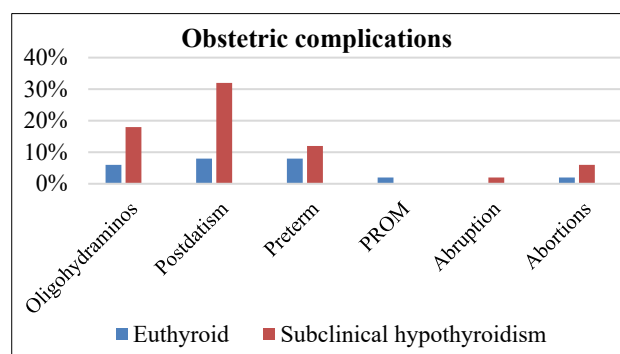
The incidence of preeclampsia among the euthyroid group of antenatal women is 4 (8%) whereas among the antenatal women with subclinical hypothyroidism, the incidence is 11 (22%). The result is statistically significant, p value being 0.02.

9 (18%) of women with subclinical hypothyroidism developed oligohydramnios as compared to 3 (6%) of

euthyroid women. The results were statistically significant (p value: 0.03). The incidence of postdatism ie gestational age was beyond 40 weeks was 16 (32%) among those of antenatal women with subclinical hypothyroidism. The incidence of postdatism among the Euthyroid antenatal women was 4 (8%). The difference among both the groups was statistically different (p value: 0.001).

Table 3: Obstetric complications.

Obstetric complications	Euthyroid (%)	Subclinical hypothyroidism (%)	Test of significance
Oligohydramnios	6	18	0.03
Postdatism	8	32	0.001
Preterm	8	12	0.26
PROM	2	0	0.25
Abruption	0	2	0.25
Abortions	2	6	0.18

**Figure 2: Comparison of obstetric complications between two groups.**

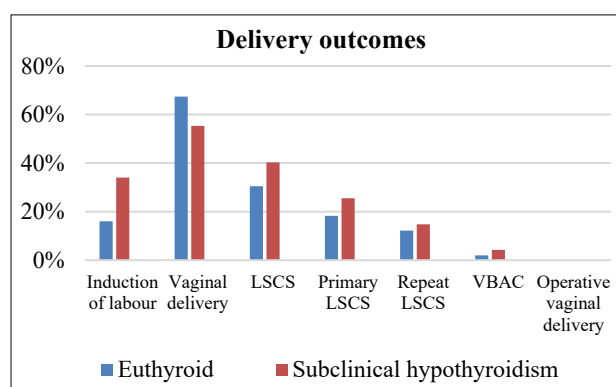
Other obstetric complications were also studied. The incidence of preterm delivery was 6 (12%) among the antenatal women with subclinical hypothyroidism as compared to 4 (8%) among the women with normal thyroid profile. There was 1 case of PROM among the euthyroid women and none among those of subclinical hypothyroidism. There was 1 case of abruption among the women with subclinical hypothyroidism and none was there among those of women with normal thyroid profile. 3 abortions cases were observed among antenatal women with subclinical hypothyroidism and 1 among euthyroid women. There was no statistically significant difference among the two groups in any of the above.

The labour induction rates were 34% and 16% in antenatal women with subclinical hypothyroidism and women with normal thyroid profile respectively and these differences are statistically significant. They had 2.7 times increased risk of being induced than euthyroid women.

Postdatism was the major reason for the induction among the antenatal women with subclinical hypothyroidism (58.82%).

Table 4: Delivery outcomes.

Delivery outcome	Euthyr-oid (%)	Subclinical hypothyroidism (%)
Induction of labour	16	34
Vaginal delivery	67.4	55.3
LSCS	30.5	40.3
Primary LSCS	18.3	25.5
Repeat LSCS	12.2	14.8
VBAC	2	4.2
Operative vaginal delivery	0	0

**Figure 3: Comparison of delivery outcomes between two groups.**

The LSCS rate was 40.3% among the antenatal women with subclinical hypothyroidism as compared to 30.5% among the euthyroid women. The difference was not statistically significant and thus the LSCS rate was not increased in antenatal women with subclinical hypothyroidism.

Table 5: Gestational age at delivery.

Gestational age at delivery (weeks)	Euthyroid (%)	Subclinical hypothyroidism (%)
<37	8.16	12.76
37-39.5	83.6	53.19
>40	8.16	34

83.6% of euthyroid women and 53.19% of subclinical hypothyroidism delivered between 37 to 40 weeks of gestation. 8.16% of euthyroid and 12.76% of subclinical hypothyroidism delivered preterm. 34% of subclinical hypothyroidism and 8.16% of euthyroid delivered postdate.

Majority of neonate born to women with euthyroid (46.9%) and women with subclinical hypothyroidism (34.0%) belong to 2.5–2.9 kg. The birthweight of neonate among the two groups are comparative, mean birthweight being 2.6 kg. There is no statistically significant difference.

Table 6: Mean birth weight.

Parameters	Mean	Standard deviation	Student t test
Euthyroid	2.6	0.47	0.34, not significant
Subclinical hypothyroidism	2.6	0.54	

Table 7: Other neonatal outcomes.

Variables	Euthyroid (%)	Subclinical hypothyroidism (%)
APGAR at 5 min {<7}	16.3	38.2
NICU admission	12.2	34
Neonatal hyperbilirubinaemia	20.41	29.78
Neonatal hypothyroidism	0	0

38.2% antenatal women with subclinical hypothyroidism have low APGAR (<7) as compared to 16.3% among euthyroid antenatal women. The difference is statistically significant with p value of 0.01.

34% of neonate born to subclinical hypothyroidism were and 12.2% neonate born to women with normal thyroid profile were admitted to NICU. The result is statistically significant. The major reason for NICU admission among antenatal with subclinical hypothyroidism was meconium aspiration and asphyxia whereas among the euthyroid women, the reason is preterm.

20.41% of the newborn born to euthyroid women developed hyperbilirubinaemia as compared to 29.78% among the newborn of women with subclinical hypothyroidism. The result was not statistically significant

None of the newborn developed neonatal hypothyroidism among the two groups.

DISCUSSION

Thyroid disease is common among the women of reproductive age group. Subclinical hypothyroidism has been associated with adverse pregnancy outcome.

In our study mean age of distribution among the subclinical hypothyroidism women is 24.67 years which is comparable to study done by Dhanwal et al where the mean age was 25.5 years.⁵ The age group in the study by Sreelatha et al was 25-30 years.⁷ However, in another study done by Gupta et al, the age group was more than 30 years.⁶ In current study, the mean BMI is 24.6±3.5 (i.e. 21.1 to 28.1) kg/m² which is comparable to Vaidya et al which is 23.9 kg/m².⁸

In our study, 20% of women with subclinical hypothyroidism had history of infertility. According to a

study by Jagun et al, the prevalence of subclinical hypothyroidism among the infertile women was 11.7%.⁹ A similar study by Verma et al suggested 62.7% of infertile female had subclinical hypothyroidism.¹⁰

In present study, anaemia in subclinical hypothyroidism patient was about 36% which is higher as compared to study done by Pavanaganga et al (5.08%) and Ajmani et al (14.1%).^{11,12}

In present study, 22% of subclinical hypothyroidism women developed preeclampsia. Ajmani et al observed similar results (22%).¹² Sarladevi et al and Sahu et al observed lower percentage of preeclampsia (9.3% and 9.8% respectively) as compared to present study.^{13,14} While Pokhanna et al noted higher percentage of preeclampsia (30%) as compared to present study.¹⁵

In present study, oligohydramnios was about 18% which is correlating with study done by Sreelatha et al (16.7%).⁷ Data regarding other maternal outcome such as gestational diabetes and postpartum is very limited in other studies.

In our study, rate of abortion was 6% which is correlating with Ajmani et al (5.5%) and Pokhanna et al (6.6%).^{12,15} In present study, preterm labour in subclinical hypothyroidism is 12% and in study by Sahu et al is 10.3% and by Ajmani et al is 11.2%.^{12,14} In a study by Tanuja et al, abortion rate was 0.3% whereas in our study only 1 case (2%) of abortion was noted.¹⁶ In present study, primary LSCS in women with subclinical hypothyroidism was 25.5% which is correlating with Sreelatha et al (22.9%).⁷ The most common cause of LSCS was induction failure (47.3%) among group with subclinical hypothyroidism.

In the present study, most common reported unfavourable neonatal outcome among subclinical hypothyroidism was NICU admission (34%) and low APGAR score (38.2%). The most common reason for NICU admission is meconium aspiration. The NICU admission in study of Sreelatha et al is 9.4%.⁷ The rate of neonatal hyperbilirubinaemia and neonatal hypothyroidism was not significantly higher as compared to control group.

Limitations

The study was conducted in a single tertiary care hospital with relatively small sample size, which may limit the generalizability of the findings to the wider population. Since antithyroid antibodies could be present in females which could have their manifestation during pregnancy and postpartum period and also have a role in causing hypothyroidism. Screening of AntiTPO antibodies was not done in our studies.

CONCLUSION

Since during 1st twelve weeks of pregnancy, the foetus entirely depends on the maternal thyroid hormone for

normal neuronal and skeletal development. Hence it is must to perform thyroid function tests in the 1st trimester. Unfavorable maternal outcome such as anaemia, preeclampsia, oligohydramnios, was statistically significantly associated with subclinical hypothyroidism. Subclinical hypothyroidism is also associated with the higher NICU admission and lower APGAR score.

Therefore, the evaluation for altered thyroid profile in early pregnancy and timely intervention for treatment will lead to decrease in all complications and will improve the maternal and also in terms of foetal outcome. In case of subclinical hypothyroidism, we can start antithyroid drugs to increase the chances of conception in case of infertility.

Since antithyroid antibodies could be present in females which could have their manifestation during pregnancy and postpartum period and also have a role in causing hypothyroidism. Screening of AntiTPO antibodies should be done which was not done in our studies.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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