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Research Article

Maternal and fetal outcome in subclinical hypothyroidism in Jammu region, North India

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ABSTRACT

Background: Pregnancy is a period that places great physiological stress on both the mother and the fetus in the best of times. The objective of this study was to study the maternal outcomes in terms of miscarriage, gestational hypertension, preeclampsia, placenta previa, placental abruption, preterm labour, preterm PROM, rate of caesarean section and postpartum hemorrhage. And to study the fetal outcomes in terms of premature birth, low-birth weight, fetal distress in labour, fetal death and congenital anomalies.
Methods: The studied subjects included all pregnant women reporting to the hospital for a period of one year November 2012 to October 2013. All participants were subjected to detailed history, thorough general physical, systemic, local examinations, and routine investigations, thyroid function tests (serum TSH, T3, T4). All participants were divided into two groups, group-I: pregnant women diagnosed with subclinical hypothyroidism (TSH 5-10Mu/L; T3 and T4 normal), group-II: euthyroid pregnant women (control group). Maternal and fetal outcomes of subjects in the first group (study) were compared with control group. The data was analyzed using computer software Microsoft Excel and SPSS version 19.0 for Windows. Chi square test was performed to evaluate statistical significance. A p-value of <0.05 was considered as statistically significant.
Results: A total of 17045 pregnant women reported to labour room and OPD and 15120 women qualified after applying exclusion criteria. Out of these, 14770 pregnant women were found euthyroid and subclinical hypothyroidism was identified in 350 (2.05%) women. Maternal outcome in study group in terms of miscarriage ($p<0.001$), gestational hypertension ($p<0.001$), placental abruption ($p<0.0001$) and preterm premature rupture of membrane ($p=0.007$) was found to be statistically significant when compared with control group, while fetal outcome in terms of fetal distress ($p<0.001$), low birth weight ($p<0.001$) and premature birth ($p=0.002$) was found to be statistically significant.
Conclusions: In view of adverse maternal and fetal outcome, detecting and treating the women with subclinical hypothyroidism in early pregnancy will improve the perinatal outcome.

Keywords: Subclinical hypothyroidism, Maternal outcome, Fetal outcome

INTRODUCTION

Pregnancy is a period that places great physiological stress on both the mother and the fetus in the best of times. However, if pregnancy is compounded by endocrine disorders such as hypothyroidism, the potential for maternal and fetal adverse outcomes can be immense. Hypothyroidism during pregnancy is usually asymptomatic, especially when subclinical. Antithyroid antibodies are prevalent in pregnancy, found in approximately 10% of women in the second trimester.[1] Thyroid disease is the second most common endocrine disorder, after diabetes mellitus, affecting women of reproductive age. The incidence of hypothyroidism

during pregnancy is estimated to be 0.3 to 0.5% for overt hypothyroidism and 3 to 5% for subclinical hypothyroidism.[2]

Thyroid physiology is perceptibly modified during normal pregnancy.[3] The most notable change is the increase in thyroxin-binding globulin (TBG). This begins early in the first trimester, plateaus during mid-gestation and persists until shortly after delivery. This is due to stimulation of TBG synthesis by elevated estrogen levels and more importantly due to a reduced hepatic clearance of TBG because of estrogen-induced sialylation.[4] This increased TBG concentration leads to an expansion of the extra-thyroidal pool and results in elevated total T3 and T4 levels due to an increase in maternal thyroid hormone synthesis. Women with hypothyroidism have decreased fertility; even if they conceive, risk of abortion is increased and risk of gestational hypertension, anemia, abruptio placentae and postpartum haemorrhage is increased.[5] The risk of these complications is greater in women with overt, rather than subclinical hypothyroidism.[3]

Untreated hypothyroidism is associated with increased risk for preeclampsia, low birth weight, placental abruption, miscarriage and perinatal mortality.[6] In addition, hypothyroidism early and late in pregnancy may also increase the rate of caesarean section.[7] Fetal thyroid is capable of trapping iodine by 12 weeks and can synthesize thyroxin by 14 weeks of gestation. Even transient hypothyroidism can cause adverse neurologic outcome in a new-born. Thus, early diagnosis and treatment is recommended.[8] The obstetric complications of hypothyroidism contribute to the overall increase in frequency of adverse neonatal outcomes, which include preterm birth, low birth weight, increased admission to neonatal intensive care and increased perinatal morbidity and mortality.[9]

Treatment of maternal hypothyroidism during pregnancy greatly improves both obstetrical and neonatal outcomes.[10-12] Women should be made euthyroid as quickly as possible. India is one of the major endemic regions of goitre in the world and Jammu And Kashmir State falls in the "Himalayan goitre belt which is world's biggest goitre belt.

METHODS

The present study was conducted in the department of obstetrics and gynaecology, government medical college, Jammu. The studied subjects included pregnant women with subclinical hypothyroidism reporting to the hospital for a period of one year November 2012 to October 2013. Pregnant women diagnosed with subclinical hypothyroidism and euthyroid pregnant women were included while pregnant women with hyperthyroidism, overt hypothyroidism, other medical disorders-hypertension, diabetes mellitus, renal disorders, etc. and drug-induced hypothyroidism were excluded. All participants included in the study were subjected to detailed history; thorough general physical, systemic, local examinations, routine investigations, thyroid function tests (serum TSH, T3, T4) and patients with altered TFT were tested for thyroid peroxidase antibodies (TPOAb).

All participants were divided into two groups, group-I: pregnant women diagnosed with subclinical hypothyroidism and group-II: euthyroid pregnant women (control group). Maternal and fetal outcomes of subjects in the first group were compared with control group. Serum TSH, T3, T4 was measured by radioimmunoassay (RIA) method. The reference values taken in the present study were as per medical college endocrinology laboratory, which are as follows: TSH (0.5 to 5 mU/L), T3 (0.8 to 1.6 ng/mL or 80 to 160 ng/dL) and T4 (60 to 120 ng/mL or 6 to 12 µg/dL).

The data was analyzed using computer software Microsoft Excel and SPSS version 19.0 for Windows. Mean and standard deviation (SD) was calculated and reported for quantitative variables. Chi square test was performed to evaluate statistical significance. A p-value of <0.05 was considered a statistically significance.

RESULTS

17045 pregnant women, reported to labour room and OPD from November 2012 to October 2013. A total of 15120 pregnant women qualified after applying exclusion criteria and 14770 pregnant women were found euthyroid. Subclinical hypothyroidism was identified in 350 (2.05%) pregnant women and further observations were made on subclinical hypothyroid women, who are as follows: majority of patients (47.15%) were in the age group of 26-30 years, (38.28%) in age group of 20-25 years. Mean age was 26.89±3.93 years with range of 20-40 years. Majority of patients (38.58%) were primigravidas, G2 (33.71%), G3 (17.43%) and G4 and above (10.28%). Majority of patients (50.29%) presented at a gestational age between 37-40 weeks, 28.85% at <20 weeks, 16% at 20-37 weeks and 4.86% at >40 weeks. Mean gestational age at time of presentation was 29.79±12.49 weeks with range of 6-40.5 weeks.

Statistically, maternal outcomes like gestational hypertension, miscarriage, preterm premature rupture of membrane and placental abruption were found to be highly significant ($p<0.01$), while preterm labour, preeclampsia, placental previa, postpartum haemorrhage and lower segment caesarean section were found to be non-significant ($p>0.05$) (Table 1).

Statistically, fetal outcomes like fetal distress, low birth weight (<2.5 kg) and premature birth were found to be highly significant ($p<0.01$), while intrauterine deaths and congenital anomalies were found to be non-significant ($p>0.05$) (Table 2).

Table 1: Comparison of maternal outcome between euthyroid and subclinical hypothyroidism patients.

Maternal outcome	Patients		
	Euthyroid (n=14770) number	Subclinical hypothyroidism (n=350) number	Statistical inference (χ^2 test)
Gestational hypertension	2441	109	p<0.001**
Miscarriage	1777	101	p<0.001**
Preterm labour	1016	21	p=0.52*
Preterm premature rupture of membrane	490	20	0=0.007**
Placental abruption	192	19	p<0.0001**
Preeclampsia	820	16	p=0.42*
Placenta previa	344	13	p=0.09*
Postpartum haemorrhage	388	11	p=0.55*
Lower segment caesarean section	5123	121	p=0.96*

*Non-significant; **Highly significant

Table 2: Comparison of fetal outcome between euthyroid and subclinical hypothyroidism patients.

Fetal outcome	Patients		
	Euthyroid (n=14770) number	Subclinical hypothyroidism (n=350) number	Statistical inference (χ^2 test)
Fetal distress	1550	69	p<0.001**
Low birth weight (<2.5 kg)	1764	66	p<0.001**
Premature birth (20-37 weeks)	1610	56	P=0.002**
IUD	546	11	p=0.58*
Congenital anomalies	280	2	0=0.70*

*Non-significant; **Highly significant

DISCUSSION

Thyroid disorders are common endocrine problems in pregnant women. It is now well established that both overt and subclinical thyroid dysfunction have adverse effect on maternal and fetal outcome. However, pregnant women with thyroid disease do not always develop symptoms, and when they do, these symptoms can sometime be attributed to pregnancy itself and can only get exaggerated. In these situations, accurate laboratory assessment of maternal thyroid function assumes a great importance.

There are several important findings from this prospective analysis of more than 17000 women. First, subclinical hypothyroidism was identified in 350 (2.05%) women and this corresponds with virtually all previous reports, Klein et al (2.4%), Glioner (2.2%), Allan et al (2.2%), Casey et al (2.3%), Aziz et al (2.5%), Vaidya et al (2.6%), Cleary-Goldman et al. (2.2% in the first and 2.2% in the second trimester) and Nambiar et al (4.8% in first trimester).[13-20]

Second in this study, women with subclinical hypothyroidism had statistically significant miscarriage rate with (p<0.001) which was reported in previous study also Negro et al, Abalovich et al showed that untreated hypothyroidism, subclinical or overt, at the time of conception is associated with miscarriage rate of 31.4% compared with 4% in euthyroid subjects at conception.[2,21] Wang et al also reported that the incidence of spontaneous abortions in the subclinical hypothyroidism group was higher than in the normal TSH group (15.48% versus 8.86%).[22]

Third, 109 (31.14%) pregnant women with subclinical hypothyroidism had gestational hypertension which was statistically significant (p<0.001). Leung et al also reported that gestational hypertension was significantly more common in the overt (22%) and subclinical hypothyroid (15%) patients than in the general population (7.6%) and Casey et al reported that gestational hypertension occurred not only in overt hypothyroidism (36.1%) but also in subclinical hypothyroidism compared to general population.[16,23]

Fourth, 19 (5.43%) pregnant women with subclinical hypothyroidism had placental abruption which was statistically significant (p<0.0001) while Casey et al reported that pregnancies in women with subclinical hypothyroidism were three times more likely to be complicated by placental abruption and it was statistically significant (p=0.026).[16]

Fifth, 20 (5.71%) women with subclinical hypothyroidism had preterm premature rupture of membranes (PPROM) which was found to be statistically significant with (p=0.007). Eight (40%) women with PPROM in subclinical hypothyroidism were positive for TPOAb and none for anti-thyroglobulin antibodies. Cleary-Goldman et al reported that preterm premature rupture of membrane was significantly increased when both antibodies were positive in either trimester.[19]

Sixth, 56 (16%) women with subclinical hypothyroidism had preterm delivery (p=0.002) and 66 (18.86%) women delivered low birth weight babies and when compared with euthyroid pregnant women (p<0.001). Idris et al performed a retrospective study of data from 167 pregnancies managed in the antenatal endocrine clinic and reported that maternal hypothyroidism at presentation and in third trimester may increase the risk of low birth weight.[7]

Seventh, 69 (19.71%) pregnant women with subclinical hypothyroidism had fetal distress during labour which was statistically significant (p<0.001). Rests of the findings were found not significant.

CONCLUSION

There is a need for early detection of hypothyroidism in early pregnancy so that adequate treatment could be started at the earliest in order to prevent poor maternal and fetal outcome. In a country like India where pregnancy rate is very high because of sheer magnitude of the population and where majority of women seek antenatal care at government institutions, diagnosing hypothyroidism at the earliest could have profound implication on the health of the nation.

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