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RESEARCH ARTICLE

PREVALENCE OF SUBCLINICAL HYPOTHYROIDISM AND ITS FOETO-MATERNAL OUTCOME IN SUBHIMALAYAN PREGNANT WOMEN

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Abstract

Background: Thyroid disorders are the most common endocrinopathies encountered during pregnancy in India. Thyroid gland and its functions are immensely influenced by pregnancy. This study was designed to evaluate the prevalence of subclinical hypothyroidism in pregnancy and its foeto-maternal outcome amongst the pregnant mothers having such disorder.

Methods: In this hospital based, observational, comparative study, which was carried out on 200 pregnant women attending secondary care hospital of subhimalayan region for the duration of 1 year (2017 to 2018).Morning blood samples of study participants were analyzed for free T4, TSH in their first trimester, and they were followed up till the time of confinement for foeto-maternal outcome.

Results: prevalence of thyroid disorder was 16% which was high as compare to other regions of India. Subclinical hypothyroidism was highly prevalent (13.5%) and masked, associated with adverse maternal outcomes like anaemia (p=0.001), abortion (p=0.012), postpartum haemorrhage (p=0.012), puerperal sepsis (p=0.008) and adverse foetal outcome like foetal growth restriction (p=0.034) as compared to euthyroidism.

Conclusion: In a developing country like India where undiagnosed thyroid disorders especially subclinical hypothyroidism is highly prevalent and associated with adverse foeto-maternal outcomes, our study recommends universal screening of pregnant women for such disorders.

Introduction:-

Thyroid disorders are the most common endocrinopathies encountered during pregnancy in India [1]. It is well established fact that overt hypothyroidism during pregnancy is deleterious to both mother and child[2,3,4]. Thyroid gland and its function are immensely influenced by pregnancy. In countries with adequate iodine sources, 10% thyroid gland enlargement may be noticed during pregnancy, and it increases even more in iodine-deficient countries[5]. During pregnancy, the yield of thyroid hormones and iodine demand each increases by approximately 50%[6]. The thyroid is under a stress test due to curbed thyroidal reserve or relative iodine deficiency leading to physiological and pathological changes in thyroid status during pregnancy.

The association between miscarriage and preterm delivery in women having normal thyroid function with positive thyroid peroxidise (TPO) antibodies, has been emphasized by data from recently published study[7]. In children born

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to hypothyroid mothers, adverse effects including attention deficit and hyperactivity syndrome have been reported[8,9]. Approximately one in ten women during their first trimester of pregnancy produce antibodies against TPO or against thyroglobulin, and in roughly 16% of these women hypothyroidism ensues. Thyroid disorder may be overlooked in pregnancy because of nonspecific symptoms and hyper metabolic state of pregnancy.

There is a wide variation in prevalence of thyroid disorders in pregnancy with respect to geography. According to the Western literature the prevalence of hypothyroidism in gestational period is roughly 2.5%[10]. Some studies on prevalence of thyroid dysfunction during pregnancy in India have shown that the prevalence rate of such disorder during pregnancy is 4.8% to 11%[11,12].

During the first trimester of pregnancy there is a brief fall in thyroid stimulating hormone (TSH) due to the structural similarity between the molecules and receptors of TSH and human chorionic gonadotropin (hCG), which leads to an increase in thyroid hormone production due to hCG stimulation of the thyroid. In pregnancy thyroid hormone concentrations in blood are increased partly due to the hyperestrogenic state of pregnancy and due to the weak thyroid stimulating effects of hCG that mimics TSH. Action of hCG is by cross reactivity of this hormone with TSH receptors[13].

Thyroid dysfunction is one of the most frequent endocrine diseases among women of reproductive age group. Hypothyroidism can be overt or subclinical[14]. Overt hypothyroidism is characterised by an elevated serum level of TSH and subnormal free T4 (fT4) concentration. Subclinical hypothyroidism (SCH) is defined as a TSH concentration exceeding the trimester specific reference value in combination with normal fT4 concentration[15, 16].

Pregnant women with normal TSH and fT4 levels are considered to be euthyroid. The trimester specific reference ranges for TSH as per guidelines of the American Thyroid Association are 0.1-2.5mIU/L in first trimester, 0.20-3.0mIU/L in second and 0.3-3.0mIU/L in the third trimester[17].

Women diagnosed with overt hypothyroidism carry high risk of pregnancy-related adverse outcomes such as threatened abortion, preeclampsia, preterm delivery, abruption placenta and postpartum haemorrhage (PPH). Foetal outcomes such as low-birth-weight (LBW), miscarriage in first trimester, preterm delivery, intrauterine growth retardation(IUGR), still birth and neonatal deaths, neonatal hyperbilirubinemia, congenital hypothyroidism, and increased incidence of perinatal death[18].

We hypothesized that SCH is associated with adverse foeto-maternal outcome in pregnancy. The spectrum of thyroid dysfunction is varied in nature. There are so many studies, which have established the obstetric and foetal complications associated with overt hypothyroidism but there is not adequate number of studies to evaluate adverse effects of SCH during pregnancy hence this study was undertaken.

Aims and Objectives:-

To detect prevalence of SCH among pregnant women attending secondary care centre and to assess the adverse maternal and foetal outcomes of pregnant mothers having subclinical hypothyroidism as compared to euthyroid pregnant women.

Materials and Methods:-

A hospital based, observational, comparative study was carried out in the department of obstetrics and gynaecology at a secondary care centre, over a period of one year from 1st February, 2017- 31st January, 2018.After approval from ethical committee the participant's voluntary informed consent was obtained after explanation of purpose, method, and course. Based on the study conducted by Dhanwal et al.[1] prevalence of SCH during the pregnancy was 13.5%, assuming the absolute precision is 5% and 95% confidence interval, the required sample size was estimated to be 179. A total number of 200 pregnant mothers primigravida or multigravida having Singleton pregnancy of <12 weeks of gestation were included in the present study.

Whereas those excluded were pregnancy with multifoetal gestation, Medical history including overt hypothyroidism, diabetes and other endocrine disorders, chronic hypertension, malignancy, autoimmune diseases, with presence of tuberculosis, AIDS, elevated liver enzyme and creatinine levels, habits like Alcoholics and smokers drug abuse, or women planning to follow up and delivery in other hospital.

All the enrolled mothers during their first trimester of pregnancy were evaluated by detailed history taking, clinical examination, routine investigations and serum TSH level and free T4 level by ELISA method. They were kept under close follow-up and they were evaluated for the development of any antenatal, intranatal, postnatal complications. Mode of delivery and development of any foetal complications were also noted.

The Statistical analysis was performed by STATA 11.2 (College station TX USA). Chi Square test goodness of fit has been used to measure the association between the maternal and foetal complications.

Results:-

Our study revealed that the prevalence of subclinical hypothyroidism was 13.5%. Incidence of antenatal complications such as anaemia and abortions were found to be significantly higher in SCH women as compared to euthyroid women (p=0.001 and 0.012). Postpartum complications like Postpartum haemorrhage (PPH) and puerperal sepsis were found significantly higher in SCH group as compared to euthyroid group (p=0.012 and 0.008). Though occurrence of hypertensive disorder in pregnancy (11.11% vs 4.17%) and antepartum haemorrhage (APH) (3.70% vs 0.60%) was higher in SCH group as compared to euthyroid group, these two parameters were not found to be significantly associated with subclinical hypothyroidism. On evaluation of foetal outcome intra uterine growth restriction (IUGR) was found to be significantly increased in SCH group as compared to euthyroid group (p=0.034). Though occurrence of still born (3.70%) was higher in SCH group as compared to euthyroid group (0.60%), but this parameter was not found to be statistically significant.

Discussion:-

The major findings of the present study were that the period prevalence of thyroid dysfunction in our study population was 16.0%. 15.5% had hypothyroidism, of which 13.5% were found to have subclinical hypothyroidism and 2.0% had overt hypothyroidism. 0.5% had subclinical hyperthyroidism and none of the women was found to have overt hyperthyroidism. Sahu MT et al.[12] reported 11.05 % pregnant women had hypothyroidism of which 6.47 % and 4.58% had SCH and overt hypothyroidism respectively. In our study prevalence of hypothyroidism and SCH are higher but overt hypothyroidism in our study was lesser as compared to their study. Vimal Nambiar et al.[11] reported prevalence of hypothyroidism and thyroid autoimmunity (TAI) was 4.8%, and 12.4% respectively. TAI and hypothyroidism were significantly associated with miscarriage. In our study the prevalence of hypothyroidism is almost four times but the thyroid autoantibody status was not checked in the present study. Dinesh K Dhanwal et al.[1] reported 14.3% pregnant women had hypothyroidism with 13.5% had SCH in their first trimester. In our study results are comparable to their study. Anagha S et al.[19] conducted a study that showed prevalence of hypothyroidism was 10.96% which is less as compared to our study finding of 15.5%. B Vaidya et al.[20], Gayathri R et al.[21] had conducted various studies independently with prevalence of thyroid dysfunction of 2.6%, 3.69%, and 2.8% respectively, which are much lesser than prevalence of the present study. Guan HX et al.[22] reported the prevalence of thyroid dysfunction 7.9% with 6.8% hypothyroidism cases and 1.1% hyperthyroidism cases. In our study the prevalence of hypothyroidism is more as compared to this study result, but the prevalence of hyperthyroidism in our study is 0.5% which is comparable to this Chinese prevalence.

In our study SCH was more prevalent and masked, because we conducted the study on the population of sub Himalayan region which is known to be zone of iodine deficiency. So, it becomes imperative to screen thyroid dysfunction in pregnant women belonging to this zone by estimation of the levels of TSH and fT4, especially in pregnant women as thyroid dysfunctions might have deleterious effect on maternal and foetal outcomes.In this study we had evaluated the occurrence of various maternal and foetal complications in SCH group and were compared to those of euthyroid group.

In our study, abortion rate was found to be 3.70% in SCH group, where as none of the women in euthyroid group was found to have this complication and this difference was found to be statistically significant (p = 0.012). Wang S et al.[23] in the year 2012 in their study showed that incidence of spontaneous abortion in the SCH group was higher than the euthyroid group (15.48% vs 8.86%, p=0.03). Similarly, Abalovich M et al.[24] found that untreated SCH and overt hypothyroidism is associated with increased miscarriage rate of 31.4% versus 4% in euthyroid subjects at the time of conception.

In our study 11.11 % mothers of SCH group and 4.17% mothers of euthyroid group had preeclampsia. Occurrence of preeclampsia was higher in SCH group as compared to euthyroid group. But it was not found to be statistically

significant when both groups were compared (p=0.129). Our study results are different from the study published by Wilson et al.[25] who showed significant association between SCH and severe preeclampsia (adjusted OR=1.6, 95% CI=1.1to2.4; p=0.03).

In our study a significantly higher incidence of anaemia among mothers with SCH as compared to euthyroid mothers was found. (29.63% vs 7.74%, p= 0.001). Sannaboraiah A et al.[26] stated that pregnant women with SCH had increased risk of developing anaemia.

The occurrence of preterm labour was not found to be significant between SCH and euthyroid group n the present study. Study done by Casey BM et al. [4] showed that preterm delivery is almost 2 folds higher in women with subclinical hypothyroidism (RR=1.8, 95% CI= 1.1 to 2.9).

In our study, occurrence of APH was higher in SCH group as compared to euthyroid group (3.70% vs 0.60%), but it was not significantly different when both the groups were compared (p=0.137). Casey BM et al.[4] showed that pregnancies in women with SCH were 3 times more likely to be complicated by placental abruption (RR-3.0, 95% CI 1.1-8.2).

In the present study occurrence of PPH was found to be 3.70% in SCH group, where as none of the women in euthyroid group was found to have this complication and this difference was found to be statistically significant (p=0.012).

Radha K R et al.[27] in their study in the year 2017 showed that incidence of PPH was higher in SCH mothers compared to euthyroid mothers (6% vs 2%, p=0.014). They also found significant association between inadequately treated hypothyroidism and maternal complications like anaemia, placental abruption, placenta previa, PPH, preterm delivery and caesarean section rate for foetal distress.

In our study we found that occurrence of puerperal sepsis in 7.41% cases of SCH group and 0.60% cases of euthyroid group and this difference was also statistically significant(p=0.008).

In our study occurrence of IUGR was found significantly different in SCH group as compared to euthyroid group (7.41% vs 1.19%, p=0.034). In a study done by Saki F et al.[28]found significant association of SCH with IUGR (p=0.028).

In our study the incidence of still born was found to be 3.70% in SCH group as compare to 0.60% in euthyroid group. Though the occurrence of stillborn was higher in SCH group as compared to euthyroid group the difference was not statistically significant (p=0.147). Ashoor G et al.[29] and Ohashi et al.[30] showed in their study that impaired thyroid function may predispose to miscarriage and foetal death.

The occurrence of LBW baby was not found to be significant between SCH and euthyroid group in the present study. Sannaboraiah A et al.[26] showed in their study that LBW was more in SCH mothers than euthyroid pregnancy with incidence of about 15.78%. There was strong association between SCH and LBW (p=0.001).

In our study incidence of birth asphyxia was not significantly associated with SCH. Our results were different from study published by Goel P et al.[31] who showed a higher risk of foetal distress in SCH group than euthyroid group.

To conclude, in a sub Himalayan region like ours where undiagnosed thyroid disorders especially subclinical hypothyroidism is highly prevalent (13.5%) and associated with adverse maternal outcomes like anaemia (p=0.001), abortion (p=0.012), postpartum haemorrhage (p=0.012), puerperal sepsis (p=0.008) and adverse foetal outcome like IUGR (p=0.034) as compared to euthyroidism.

We recommend that 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, a simple screening tool to measure thyroid function if made available has profound implications on the health of the nation.

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