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# Pregnancy Outcome in Treated Maternal Hypothyroidism: An Observational Study

*Rajan* Sankar, *Gopalakrishnan* Sripathy, *Tarun* Sekhri, *Walia* RP, *Shushil Kumar* Jain
*Thyroid Research Centre, Institute of Nuclear Medicine and Allied Sciences, Defence Research and Development Organisation, Lucknow Road, Delhi – 110 054.*

**OBJECTIVES** – To study the pregnancy outcome in appropriately managed hypothyroidism. **METHODS** – This prospective observational study was carried out in a tertiary referral center for thyroid disorders. A total of 36 women with established diagnosis of primary hypothyroidism prior to pregnancy who were on regular follow up at our center were studied during pregnancy and for one year postpartum. **RESULTS** – The mean age was 27.6 ± 4.2 years. The mean dose of levo-thyroxine at presentation was 113 ± 9 µg/day and this rose to 180 ± 5.7 µg/day and the increment in the dose was found to be significant ($p<0.01$). The mean post partum levo-thyroxine dose was 140.7 ± 7 µg/day. During antenatal period, two women (5.1%) developed pregnancy-induced hypertension. No peripartum or postpartum complication developed. The mean birth weight was 2815±1.19 kg and the apgar score was above eight in all new born. On follow-up, the developmental milestones of the babies were found to be normal. **CONCLUSION** – If the hypothyroid women are appropriately managed with optimal levo-thyroxine replacement during pregnancy, the pregnancy outcomes for the mother and fetus are unaffected by hypothyroidism.

**Key words** – hypothyroidism, pregnancy outcome

## Introduction

Thyroid disorders are common endocrinopathies in women, and affect 0.2% of all women[1]. Hypothyroidism is the most common thyroid disorder in women. Maternal thyroid dysfunction may compromise both maternal and fetal well being. When hypothyroid women become pregnant, they have an increased risk of obstetric complications, including intrauterine fetal demise, gestational hypertension, placental abruption, and a poor perinatal outcome[2,3]. Although these complications of hypothyroidism have been known for quite some time, several recent publications have drawn attention to the potential fetal and neonatal repercussions of maternal thyroid hypofunction during pregnancy.

Earlier it was assumed that the placenta acts as a barier preventing maternal iodothyronines from reaching the fetus, due to poor permeability of fetal membranes and active deiodinating mechanisms[4]. Recent studies now clearly point to a role for the maternal thyroid hormone in fetal brain development and that this transfer is critical[5,6].

Since fetal thyroid becomes functional only by 16-20 weeks of gestation, maternal thyroxine levels may play a critical role in neurological development of the fetus, especially during the first trimester[7]. Since maternal thyroxine concentration in early gestation is considered important for neurodevelopment of progeny, outcome of pregnancy in women already receiving thyroxine for preexisting hypothyroidism assumes significance. Earlier studies had opined that maintenance dose of thyroxine rarely required increments during pregnancy. Recent studies have confirmed that thyroxine requirement of women with preexisting hypothyroidism increases during pregnancy[8].

Ours is a tertiary referral center that caters to the needs of patients with thyroid disorders. The present study was initiated in 1996 to evaluate the outcome of pregnancy in women with primary hypothyroidism when managed optimally throughout pregnancy. The aim was to record the maternal complications and pregnancy outcome, and to find out whether there was need to increase the dose of thyroxine during pregnancy.

## Material and Methods

Patients with hypothyroidism are followed up annually at our clinic. Women with hypothyroidism, who are in the reproductive age group are advised to report once they have a confirmed pregnancy. Such women usually report about pregnancy within 10-12 weeks of gestation. Only those women who reported within 14 weeks of gestation were included in this study.

Forty-six consecutive women with primary hypothyroidism were recruited for the study while in

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Correspondence :
Col. Rajan Sankar (Retd)
104, Mall Road, Mall Apartment,
Delhi - 110 054.
Tel. 011 23812929

the first trimester of pregnancy. They had been adequately treated with thyroxine to maintain the thyrotropin within the normal range. For analysis, thyrotropin level at the time of patient's last visit before conception was considered as pre-partum value. At each trimester, clinical parameters were recorded. Thyroid hormone (Free T4) and thyrotropin level were also measured in each trimester and antithyroid antibodies were measured in the first trimester and also once in the third trimester. Thyroxine dose in all these women was adjusted when serum thyrotropin exceeded the normal range for pregnancy.

Blood glucose estimations were done to exclude / establish gestational diabetes. Thyroid function tests were done within 8-12 weeks postpartum to analyze post-partum thyroid status and to adjust the dose of thyroxine.

Information regarding obstetric complications, mode of delivery, postpartum events of mother and parameters of newborn like apgar score at one and five minutes, head circumference and congenital anomalies were sought on a proforma from the obstetric specialists attending to these patients. The children were followed up once in three months in our clinic for at least one year. A total of 36 women had completed the follow up and were included for the final analysis.

Serum free T4 was measured by radioimmuno assay and thyrotropin by immunoradiometric assay. Antithyroid antibodies were measured using hemagglutination method.

**Results**

The mean age was 27.6 ± 4.2 years (range 19 to 34 years). Three were primigravidas, eight others had one living child and the remaining had more than one child.

All these patients were known cases of primary hypothyroidism and were on optimal thyroxine replacement therapy. The underlying cause for hypothyroidism in all of them was chronic autoimmune thyroiditis. The thyroid autoantibody (Amc) titre measured in pregnancy decreased in 28 patients, remained the same in six and increased in two.

The mean dose of thyroxine at presentation was 113 ± 9 µg per day. Patients were regularly monitored for development of pregnancy-induced hypertension and other obstetric complications. Free T4 and thryotropin estimations were done in every trimester to adjust the dose of thyroxine. Dosage was increased to maintain serum thyrotropin within normal range and free T4 at high normal level.

Mean dose of thyroxine during pregnancy rose from 113.9 µg per day to 180 ± 5.7 µg per day and this difference was highly significant ($p < 0.01$). Thyroid function tests were repeated after delivery and the mean postpartum thyroxine requirement was found to be 140.7 ± 7 µg per day and this decrease from gestational dosage was highly significant ($p<0.01$).

During antenatal follow up two patients (5.5%) developed pregnancy-induced hypertension, which was managed with appropriate antihypertensive medication. There were no miscarriages or abruptio placentae. Delivery was by cesarean section for obstetric indications in nine women (29%). Twenty-one women (67.7%) delivered normally at term, while the information regarding the mode of delivery was not available in the remaining six. Postpartum period was uneventful in all the women.

All babies had apagar score of above eight at 1 minute. None of them were reported to have major or minor congenital anomalies. Mean birth weight was 2.815 ± 1.19 kg. Babies were followed up for one year and the physical parameters and developmental milestones were found to be normal.

**Discussion**

The ready availability of sensitive thyrotropin assay has helped fairly accurate assessment of thyroid status. This has resulted in lower replacement doses of thyroxine for hypothyroidism than were employed previously. Hypothyroidism as well as uncorrected elevation in thyrotropin concentration can be clinically important and can adversely affect the outcome of pregnancy in women. Since the pregnant state imposes an extra demand on thyroid reserve in euthyroid women, it is appropriate that women being treated for hypothyroidism need to be monitored during pregnancy for adjustment of dosage[9]. Our study followed up 36 women whose hypothyroidism was optimally corrected prior to conception (as evidenced by preconception thyrotropin status). This ensured that elevation in thyrotropin level during pregnancy was due to increased requirement. At presentation the mean thyroxine dose (preconception) was 113±9 µg per day, which is comparable to that reported by Mandel at al[10]. Since thyroid function was measured at various intervals after conception, the correct period of gestation at which the thyrotropin increased could not be established. But mean dosage rose to 180 ±5.6 µg per day during pregnancy and the increase was found to be significantly higher compared to the preconception dose ($p<0.01$). When the thyroxine dose was adjusted postpartum by thyrotropin estimation, the mean dosage was reduced to 140±7.2 µg per day. Whether the magnitude of increase in dosage has any correlation with the cause of hypothyroidism could not be looked into in our study. Our findings

are similar to the results of Mandel et al[10], who also found an increased need for thyroxine during pregnancy. In our study 2 out of 36 (5.5%) women had pregnancy induced hypertension. No other complication was reported. Davies et al[11] reported a high incidence of complications in hypothyroidism in pregnancy – pregnancy induced hypertension 44%; postpartum hemorrhage 16% and still births 11%. They concluded that overt thyroid deficiency is associated with adverse pregnancy outcome. Hence it can be deduced that adequately managed hypothyroidism will reduce pregnancy related complications. When neonatal parameters were analyzed, apgar score was more than 8 at one minute in all babies regardless of the mode of delivery. Perinatal losses were reported to be higher in earlier studies, but a recent study reported a perinatal survival of 85%[3]. In our study where the hypothyroidism was monitored and optimally corrected the mean birth weight was 2.815 ± 1.19 Kg. No clinically evident congenital anomaly was detected in these babies. Although neurodevelopment was not studied systematically milestones were apparently normal.

Pop et al[12] studied neurodevelopment of children born to mothers after uncomplicated pregnancies and correlated it with maternal free T4 at 12 and 32 weeks of gestation and concluded that free T4 concentration below the 10th percentile was a significant risk factor for impaired psychomotor development.

Haddow et al[13] also found that women with high serum TSH in the second trimester of pregnancy had babies who did not perform as well on Weschler Intelligence Scale compared to matched control babies. Both these studies imply that maternal thyroid function is crucial for early neurodevelopment of the pregnancy. This is supported by studies, which show that maternal free thyroxine reaches the fetus[5].

Glinoer et al[14] found an increased demand for thyroxine in the first trimester of pregnancy and suggested that the thyroid gland is stimulated to meet this demand. In normal pregnancy, during first trimester, free T4 concentration is higher and thyrotropin level lower than in non-pregnant women[15]. The increase in T4 production in the first trimester appears to be due to a concmitant rise in HCG level. Since this physiologic augmentation of thyroxine output cannot occur in women with hypothyroidism, the demand cannot be met resulting in rise in thyrotropin level. The sustained increase in demand for thyroxine during late gestation might be due to metabolism by fetoplacental unit. In view of the above observations, close monitoring and adjustment of thyroxine dosage in pregnancy would reduce the pregnancy related complications and help to ensure normal development of the progeny.

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