

Original Research Article

Maternal hypothyroidism and neonatal outcome

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ABSTRACT

Background: Hypothyroidism is widely prevalent in pregnant women and the rate of detection, especially in a developing country like India, has not kept pace with the magnitude of the problem. The present study was conducted to evaluate thyroid function in neonates born to mothers with hypothyroidism.

Methods: A prospective observational study was conducted in KIMS Hospital Tertiary care center for 6 months. A total of 106 neonates born to mothers with hypothyroidism were included in the study. Thyroid functions of these babies were assessed at 72 hours of life.

Results: In present study, 11.8 % of mothers were hypothyroid of which 87 % were subclinical hypothyroidism and 13 % of overt hypothyroidism due to adaptation of universal screening rather than targeted screening for hypothyroidism which would otherwise go unrecognised and untreated.

Conclusions: All the babies had normal TSH and T4 levels which was probably due to early diagnosis and timely initiation of treatment to the mothers with hypothyroidism.

Keywords: Maternal hypothyroidism, Neonate, Thyroid function tests

INTRODUCTION

Hypothyroidism is widely prevalent in pregnant women and the rate of detection, especially in a developing country like India, has not kept pace with the magnitude of the problem. Since hypothyroidism is easily treated, timely detection and treatment of the disorder could reduce the burden of adverse fetal and maternal outcomes, which are very commonly encountered.

Pregnancy influences thyroid function in multiple ways. Maternal hypothalamic-pituitary-thyroid (HPT) axis undergo a series of adjustments, fetus develops its own HPT axis and the placenta plays an active role in iodide and T4 transport and metabolism. Thus, an integrated three-compartment thyroid model exists during gestation.¹ Early in pregnancy estrogen promotes production of a more highly sialylated T4-binding

globulin isoform that is less rapidly degraded, resulting in increased serum T4-binding globulin and T4 concentrations. The thyroxine-binding globulin (TBG) begins to increase early in the first trimester, plateaus during midgestation, and persists until shortly after delivery. This increased TBG concentration leads to an expansion of the extra-thyroidal pool and results in elevated total T3 and T4 levels. A high circulating HCG level in the first trimester leads to HCG cross-reactivity with the TSH receptor, resulting in temporary increase in free T4 and partial suppression of TSH. The final physiologic change results from placental deiodination of maternal T4, which increases T4 turnover.²

In normal pregnant women, the thyroid gland maintains euthyroidism with only minor fluctuations in serum T4 and TSH. However, in women with limited thyroid reserve, due to thyroid autoimmunity or iodine

deficiency, hypothyroidism can develop. Maternal hypothyroidism is diagnosed in 0.3%- 10% of pregnant women.^{3,4} Overt hypothyroidism is diagnosed in ~2.5% of otherwise normal pregnancies.⁵ Congenital hypothyroidism can be caused due to thyroid dysgenesis, disorders of thyroid hormone synthesis, iodine deficiency or excess, as well as trans-placental transfer of maternal antibodies or medications.^{3,6}

Untreated hypothyroidism is associated with several complications, most notably preeclampsia, abruptio placentae and increased risk of spontaneous miscarriage, perinatal mortality, preterm delivery and low birth weight. Treatment of pregnant mothers with l-thyroxine reduces these complications substantially.⁷ Enough evidence has accumulated over the years about the role of thyroxine in normal development of the fetal brain. Congenital hypothyroidism is a preventable cause of intellectual disability. Hence it is important to monitor babies born to mothers with hypothyroidism.

The aim of present study was to assess neonatal outcome of babies born to hypothyroid mothers.

METHODS

A prospective observational study was conducted by collecting data from March 2017 to August 2017. Maternal history, thyroid function tests and treatment details were obtained from maternal records and newborn babies' T4, TSH measured at 72 hours of life was taken as per universal neonatal screening guidelines.

Venous sample for TSH and T4 estimation was drawn and serum was processed within 24 hours of collection of sample.

Inclusion criteria

Infants born to mothers with Hypothyroidism.

Exclusion criteria

- Congenital anomalies
- Preterm Infants and sick neonates

All pregnant mothers were being screened for hypothyroidism before 18 weeks of gestation and mothers with evidence of hypothyroidism were included in the study. Trimester-specific reference interval for thyroid function tests was taken and for TSH it was as follows: 0.05-4.24, 0.13-3.95, and 0.20-3.00 uIU/mL in each trimester respectively (ATT guidelines 2017). Details regarding maternal treatment was obtained from maternal records.

Normal thyroid function tests levels were defined as- T4 8.2-19.9 mcg/dL, TSH 1.0-17.6 mIU/L in term babies according to the recent guidelines (Nelson textbook of pediatrics). Data were collated using a specific database

generated using Microsoft Excel 2010 and also analysed using program software therein.

RESULTS

All pregnant mothers (897) were screened for Hypothyroidism before 18 weeks of gestation as per standard protocol (American Thyroid Association 2017 guidelines) followed in our institution. 106 (11.8%) mothers were found to have hypothyroidism. Term new born babies of these mothers were included in the study.

87% (93) of the mothers were diagnosed to have hypothyroidism for the first time during present pregnancy. 13% (13) of the mothers were known case of hypothyroidism and on regular treatment.

67% (72) of the mothers were Primi and 33% (34) mothers were Multigravida. Of the 106 mothers 29 mothers had obstetric complications like pregnancy induced hypertension (7 mothers), gestational diabetes mellitus (6 mothers), previous LSCS (16 mothers). Among 106 mothers who received l-thyroxine treatment, 5 mothers received 100 mcg of thyroxine tablets, 23 mothers received 75 mcg, 72 were on 50 mcg and 6 were on 25 mcg of thyroxine.

Among them 65% (69) of the mothers delivered vaginally and 35% (37) of the mothers delivered through lower segment cesarean section. Indication for Cesarean section was found to be repeat section in 14 cases, cephalopelvic disproportion in 6 cases, fetal distress in 9 cases, meconium stained amniotic fluid in 8 cases.

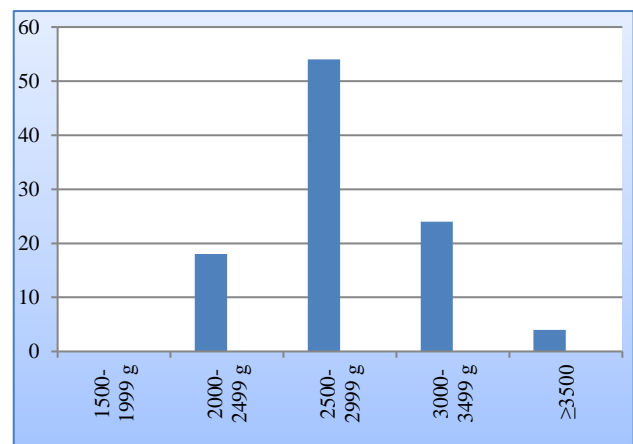


Figure 1: Distribution of birth weight.

Birth-weight was normally distributed (Figure 1). None of the babies had overweight. Low birth weight babies (<2500g) were found to be 18 (16%) babies. 4 percentage babies had birth weight more than 3500g.

Forty nine (46%) babies were found to have TSH levels ranging from 2.5-5.5 mIU/L, fifty seven (54%) babies had TSH levels, ranging from 5.5-10 mIU/L (Normal

values TSH 1.0-17.6 mIU/L) with a mean TSH 6.8 mIU/L.

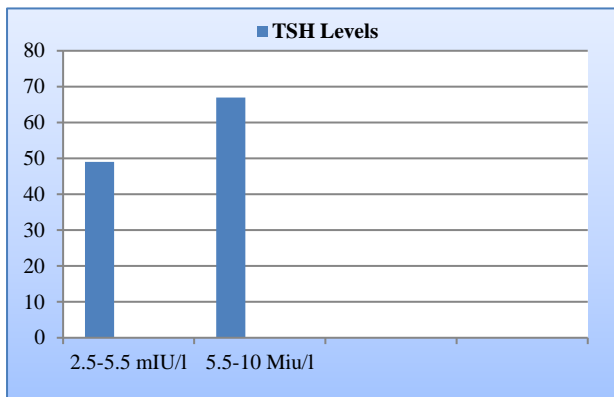


Figure 2: Newborn TSH levels.

Thyroxine levels of all the infants ranged from 9-13 mcg/dL (Normal values of T4 8.2-19.9 mcg/dL) with a mean T4 value of 11.2 mcg/dL. Since all the babies had normal TSH and T4 levels none of the infants were commenced on thyroid replacement therapy.

DISCUSSION

Congenital hypothyroidism is a serious condition that is being screened as part of the National Newborn Screening Programme. In this study we did not identify any additional infants that had clinically significant low birth weight, overweight babies, abnormal thyroid function test among babies born to mothers with hypothyroidism. This could be probably a result of mothers being screened early and early initiation of appropriate treatment.

In a systematic review by Maraka S et al among pregnant women with subclinical hypothyroidism, it was found that they were at higher risk for pregnancy loss, placental abruption, PROM, and neonatal death compared with euthyroid pregnant women. This emphasizes the importance of screening all the mothers for hypothyroidism.⁸

Effects of maternal hypothyroidism on fetal brain development are not well defined, several recent reports indicate that IQ is modestly affected (24-26). These studies have increased the concern that even mild hypothyroidism can interfere with normal brain development. Indeed, several authors have proposed screening programs for thyroid dysfunction during or even before pregnancy.

In a study done by Chang-Qing Gao et al it was found that pregnant women with subclinical hypothyroidism (SCH) had increased risks of gestational hypertension and PROM, and their fetuses and infants had increased risks of IUGR and LBW. Thus, routine maternal thyroid function testing is necessary to improve maternal and

perinatal outcomes. Untreated maternal hypothyroidism can lead to preterm birth, low birth weight, and respiratory distress in the neonate. Enough evidence has accumulated over the years about the role of thyroxine in normal development of the fetal brain.⁹ In present study all pregnant mothers were screened for hypothyroidism before 18 weeks of gestation hence neonatal outcomes were good.

Derksen-Lubsen et al in a meta analysis suggested that at least part of the brain damage in patients with CH was caused in utero and may not be prevented by initiation of early treatment after birth. All studies analyzed by them had shown a trend toward lower IQ and poorer motor skills in congenital hypothyroidism patients compared with controls; meta-analysis showed the deficit to be significant. The most important independent risk factor for the eventual outcome was the severity of congenital hypothyroidism (defined by initial T4 at the moment of diagnosis and skeletal maturation). However, two changes in management, early initiation of treatment, and higher dose l-thyroxine therapy to mother may abrogate or ameliorate any impact of thyroid hormone deficiency on intellectual development.¹⁰ This explains need for screening of all pregnant mothers for hypothyroidism in early part of gestation.

Thyroxine dose requirement increases during pregnancy and thus close monitoring of thyroid function with appropriate adjustment of thyroxine dose to maintain a normal serum TSH level is necessary throughout gestation. Within a joint endocrine-obstetric clinic, maternal hypothyroidism at presentation and in the third trimester may increase the risk of low birthweight. In this study low birth weight was found to be seen in 16 babies (18%).

Klein et al, found that serum TSH level greater than 6 mIU/L was present in 2.5% (49 of 2,000) of women at 15-18 weeks gestation. Overt hypothyroidism (i.e. an elevated serum TSH plus a T4 2.5 sd below the mean or lower) was present in 0.3% of women.¹¹ In present study we found that mean TSH value was found to be 6.8 and T4 was 11.2. 106 (11.8 % of the mothers were diagnosed to be hypothyroid and of which 87% (93) of the mothers had subclinical hypothyroidism and were diagnosed for the first time during current pregnancy and 13% (13) of the mothers were known case of hypothyroidism and on regular treatment.

Rovet reported the long-term outcome in a large cohort of Toronto based children with congenital hypothyroidism identified by newborn screening from infancy to adolescence. Early findings revealed a 5-10-point decline in IQ, poorer visuomotor and visuospatial abilities, delayed speech and language development, selective neuromotor deficiencies, and poorer attention and memory skills, which were correlated with different disease and treatment factors. Furthermore, 30% of these

adolescent patients were not receiving an adequate l-thyroxine dose.¹²

In some studies, infants and toddlers whose mothers had reduced serum free T4 concentrations (with normal TSH) during gestation (12 to 20 weeks) had lower mean intelligence, psychomotor, or behavioral scores compared with children born to women with normal thyroid function during gestation. While some studies have shown to have benefit from levothyroxine treatment of isolated hypothyroxinemia during pregnancy, on pregnancy outcome or subsequent infant development, some other studies have shown no benefit. In a study done by Casey BM et al, they study population concluded that treatment for subclinical hypothyroidism or hypothyroxinemia beginning between 8 and 20 weeks of gestation did not result in significantly better cognitive outcomes in children through 5 years of age than no treatment for those conditions.¹³

In a study by Jayaraman et al on pregnancy outcomes with thyroxine replacement for subclinical hypothyroidism they found that adverse pregnancy outcomes were not different with adequate thyroxine replacement for pregnant women with subclinical hypothyroidism targeting TSH in euthyroid range, irrespective of thyroid autoimmunity status.¹⁴

The "Controlled Antenatal Thyroid Screening Study," (CATS) by Lazarus et al, in the United Kingdom, in their ongoing 8-year prospective intervention trial seeks to determine whether universal screening of pregnant women (and levothyroxine treatment, when hypothyroid) prevents adverse outcomes. In their study, serum samples were obtained before 16 weeks gestation, with half of the sera analyzed immediately for free T4 and TSH, and the other half frozen until delivery. Women with a free T4 below the 2.5th percentile and/or TSH above the 97.5th percentile were given levothyroxine therapy. The main outcome measure was development of the unborn child, measured at 3 year of age. With the data available till date universal screening of all pregnant mothers is better than case finding so as to not miss any mother with hypothyroidism thus preventing adverse maternal and fetal outcome.¹⁵

A study of three year's duration from the UK, which followed 406 infants who had TFTs checked due to maternal thyroid dysfunction, did not identify any infants requiring thyroid replacement therapy for thyroid dysfunction.¹⁶ However, one Italian study reports prospectively following infants of mothers with hypothyroidism (secondary to autoimmunity) with TFTs over the 1st month of life.¹⁷ Three out of 129 of these infants had thyroxine therapy initiated based on mild TSH elevation (range 10.5-13.6 IU/L) at either 2 or 4 weeks of age. All three discontinued thyroxine treatment permanently between year one and two of life. Neuropsychological evaluation of these infants was normal using Griffith's scale 4 years of age.

This study was similar to UK study where none of the babies born to hypothyroid mothers required treatment with thyroxine due to early detection and initiation treatment of the mothers.

Limitation of present study being TPO antibodies could not be done for hypothyroid mothers due to non availability within the hospital and follow up IQ assessment could not be done.

CONCLUSION

In this study, 11.8 % of mothers were hypothyroid of which 87 % were subclinical hypothyroidism and 13 % of overt hypothyroidism due to adaptation of universal screening rather than targeted screening for hypothyroidism which would otherwise go unrecognised and untreated. In present study none of the babies born to these hypothyroid mothers required treatment due to early intervention during pregnancy.

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Conflict of interest: None declared

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

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