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IQ SCORES OF CHILDREN EVALUATED BETWEEN AGES 4 AND 14.5 YEARS BORN TO WOMEN WITH SUBCLINICAL HYPOTHYROIDISM WERE SIMILAR TO THE IQS OF CHILDREN BORN TO EUTHYROID TREATED WOMEN

Behrooz HG, Tohidi M, Mehrabi Y, Behrooz EG, Tehranidoost M, Azizi F. **Subclinical hypothyroidism in pregnancy: intellectual development of offspring.** Thyroid 2011;21:1143-7.

SUMMARY

BACKGROUND

The effects of maternal subclinical hypothyroidism (M-SCH) on the neuropsychological development of the offspring are not clear. Neuropsychological deficits in the offspring have been observed in overt maternal hypothyroidism and in infants born to mothers with isolated hypothyroxinemia during the first trimester of pregnancy. In one study, even when pregnant women with hypothyroidism were insufficiently treated with levothyroxine (L-T_4), the intelligence quotient (IQ) scores of their offspring were not different from those of controls. The authors evaluated the intellectual development of children of mothers who had M-SCH while they were pregnant with these children.

METHODS

A total of 62 children born to women with hypothyroidism were recruited. After excluding those <4 years or >15 years of age, 44 children were enrolled in the study. The mothers of these children were part of a subgroup of 90 women with 106 pregnancies out of 441 women with hypothyroidism who were of reproductive age seen in Tehran Endocrine Clinics between 1991 and 2003 and who were observed during gestation. Mothers were receiving L-T_4 before gestation, and their serum thyrotropin (TSH) was kept at ≤2.5 μIU/ml before conception. There were 10 miscarriages. In 2007, a total of 62 children (65%) born to these mothers were recruited for this study. Eighteen children were excluded because they were <4 years or >15 years of age. The remaining 44 children were divided into two groups, based on the mother's serum TSH values during pregnancy: TSH ≤3 mU/L on at least on two occasions in the first half of pregnancy (control group [n = 19]) and TSH >3 mU/L on at least two occasions in the first half of the pregnancy (n = 25), of whom 19 had SCH, and 6 clinical hypothyroidism. One serum TSH >3 mU/L had been detected in each mother of the case group before the 10th week of gestation. Serum TSH and free thyroxine (T_4) and urinary iodine were measured in each child, and seven cognitive performance and IQ tests were performed.

RESULTS

The 19 children of women with subclinical hypothyroidism were compared to the 19 children of euthyroid mothers. The mean age of children was 7.8 years, with a range of 4.0 to 14.5. Case children were similar to control children with respect to sex, age, parental education, maternal age at time of pregnancy and at the time of being diagnosed with hypothyroidism, percentage of mothers with thyroid peroxidase antibodies, mother's L-T_4 dose during pregnancy, gestational age at delivery, birth weight, and duration of breast-feeding. Maternal TSH (mean ±SD) in the subclinical hypothyroid case group during pregnancy was 11.3±5.3 mU/L (range, 3.9 to 27.0) and 1.4±1.0 (0.1 to 2.8) in the controls (P<0.001). Maternal T4 during pregnancy was 9.0±2.1 μg/dl (7.1 to 12.0) in hypothyroid cases versus 11.7± 2.6 (7.6 to 14.3) in controls (P<0.001). Serum TSH, free T_4, and urinary iodine concentrations were similar in the two groups of children. Total IQ, performance IQ, and verbal IQ were similar—20±14, 117±12, and 121±16, respectively, in the case group and 121±11, 120±7, and 117±15 in the control group. Results of cognitive performance tests were similar in the two groups. No relationships were observed between variables and IQ except for the education level of the mother and neonatal weight.

CONCLUSIONS

IQ level and cognitive performance of children born to women with hypothyroidism who were treated with L-T_4 are similar in those whose mothers have M-SCH during pregnancy and those whose mothers have normal serum TSH concentrations during pregnancy.

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ANALYSIS AND COMMENTARY

Maternal and obstetrical complications and impaired neurologic development in children of mothers with thyroid deficiency have been reported in the past 15 years, although results in the final outcomes are not consistent when studies are compared (1). There are many constraints when assessing and comparing published studies, among them lack of consistency in patient selection, methods of thyroid-function testing, reference ranges in defining thyroid dysfunction, iodine status in a given population, and interpretation of outcomes based on only one thyroid test value at a given gestational age. Few published studies correlate obstetrical events with outcomes in newborns. Although universal screening is not recommended by endocrine and obstetrical societies (2, 3), targeting screening of women at risk for thyroid dysfunction is encouraged, but up to 70% of women with thyroid dysfunction will be missed if targeting screening is used (4). One of the most serious potential complications reported is reduction in IQ scores in children born to women with mild hypothyroidism, reported initially by Haddow et al. (5). In their retrospective study, 62 women, whose thyroid tests were measured at 14 to 16 weeks of gestation, had serum TSH above the 97th percentile; 14 of these women were on L-T_4 therapy at the time blood was drawn and supposedly continued with the same dose during their pregnancies, and 48 of them did not receive levothyroxine treatment. The IQ score of the 62 children, evaluated between 7 and 9 years of age was not significantly different from the IQ score of 124 control children. However, a 7-point decrease in IQ scores was detected in the 48 children whose mothers with hypothyroidism did not benefit from thyroid therapy; 19% of them had IQ scores of less than 85%. This suggests that untreated mothers with perhaps more severe thyroid hypofunction were at higher risk to have children with neuropsychological impairment than were mothers who were receiving therapy, albeit still insufficient to normalize their serum TSH. In the present study by the Azizi group, the authors carefully selected women with hypothyroidism who were receiving thyroid therapy before conception, with the aim to keep their serum TSH ≤2.5 mIU/L before conception, as recommended by recent guidelines (2, 3). However, at time that pregnancy was confirmed, 25 of 44 women with hypothyroidism (56.8%) who were taking L-T_4 at conception had a serum TSH >3.0 μIU/ml , which supports the finding of the study by Abalovich et al. (6) that a serum TSH ≤1.3 μIU/ml before conception is necessary in the majority of women with hypothyroidism who are on L-T_4 therapy in order to achieve a serum TSH ≤2.5 mIU/L at the time of the first obstetrical visit. The total IQs of the children of the 19 women with subclinical hypothyroidism, as well as the performance and verbal IQ scores, were not significantly different from those of the control group, which consisted of children of mothers with a serum TSH <3 mIU/L at the first obstetrical visit. No information is given about the 6 children whose mothers had clinical hypothyroidism. A report from the Controlled Antenatal Thyroid Screening (CATS) (7) study was presented at the most recent ATA meeting by John Lazarus; it suggested no difference in IQ scores in children of women with hypothyroidism at 4 years of age irrespective of whether they received thyroid supplementation during pregnancy. These studies will encourage further discussion among those for and those against universal thyroid screening in pregnancy. Randomized, controlled studies are urgently needed in order to guide physicians concerning when and how (which thyroid tests) to use to evaluate women of reproductive age and what is the proper medical management.

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