News and Views

Maternal Graves's Disease and Neonatal Hypothyroidism

Neonates born to mothers with Graves' disease (GD) were at high risk of neonatal hypothyroidism if their mothers had high serum free thyroxine (fT4) and thyrotropin receptor autoantibodies (TRab) levels in the third trimester compared to mothers who delivered euthyroid newborns, says a new research published in the journal *Thyroid*.[1]

Researchers enrolled 305 pregnant women with Graves' disease who delivered at a hospital in Tokyo between August 2005 and May 2022. Of these, 242 women were treated with propylthiouracil (PTU) and 63 received methimazole. Umbilical cord thyroid stimulating hormone (TSH), fT4 and TRAb levels were measured at delivery. Maternal thyroid profile (free T4, TSH receptor antibodies) and daily antithyroid drug doses were assessed all through the pregnancy and at delivery. Data for the study was obtained from the hospital medical records of the participants. Through this study, the researchers aimed to determine if neonatal hypothyroidism at delivery and maternal fT4 levels, TRAb levels, and daily ATD doses during pregnancy were correlated.

The rates of neonatal hypothyroidism at delivery, which was the primary study objective, were comparable between the two groups. Nearly 13% infants born to mothers taking PTU had neonatal hypothyroidism; among infants born to mothers on methimazole, the incidence was 19%. In the PTU group, one newborn had neonatal goiter and two needed levothyroxine treatment.

The daily dose of the antithyroid drug was found to have the strongest association with neonatal hypothyroidism at delivery, the cut-off dose predictive of neonatal hypothyroidism was 150 mg/day for PTU and 10 mg/day for methimazole.

The cut-off dose of antithyroid drugs for neonatal hypothyroidism risk were determined, based on maternal TRAb levels. The cut-off PTU dose remained the same at 150 mg/day when the TRAb level was >3 times the upper limit of the normal during the third trimester, the cut-off dose increased to 20 mg/day for methimazole.

Compared to women on methimazole who delivered euthyroid newborns, those who delivered newborns with hypothyroidism were on higher doses of methimazole at 20-28 weeks of gestation (17.5 mg/day vs 10 mg/day) and 28-36 weeks (15 mg/day vs 5 mg/day). They also had lower free T4 levels at delivery (0.93 ng/dL vs 1.4 ng/dL). Similarly, in the PTU group, women with hypothyroid newborns were on higher PTU doses at 20-28 weeks of gestation (200 mg/day vs 75 mg/day) and 28-36 weeks of gestation (200 mg/day vs 50 mg/day). However, their TRab (6.1 IU/L vs 3 IU/L) and free T4 (1.48 ng/dL vs 1.12 ng/dL) levels were higher.

With each 5 mg increase in the dose of methimazole at 28 to 36 weeks of gestation, the likelihood of neonatal hypothyroidism nearly doubled with an odds ratio of 1.9. With each 50 mg increase in the dose of PTU, the probability of neonatal hypothyroidism increased slightly more than 2-folds with OR of 2.3.

This study has for the first time identified factors that were predictive of neonatal hypothyroidism at birth. Mothers with Graves' disease who delivered hypothyroid newborns had high TRab and free T4 levels in the third trimester indicating high maternal disease activity for which they needed high daily doses of antithyroid drugs. Active maternal Graves's disease therefore can be considered as a risk factor for neonatal hypothyroidism. Such women should be carefully monitored all through the pregnancy and at delivery. Measurement of TRAb and free T4 levels in the mothers in the third trimester and cord blood TSH, fT4 and TRAb at delivery may help identify newborns at risk of neonatal hypothyroidism.

Reference

1. Yoshihara A, Noh JK, Inoue K, Watanabe N, Fukushita M, Matsumoto M, et al. Incidence of and risk factors for neonatal hypothyroidism among women with graves' disease treated with antithyroid drugs until delivery. Thyroid. 2023;33(3):373-79.

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