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PRETERM BIRTH IS ASSOCIATED WITH SUBSEQUENT HYPOTHYROIDISM IN ADULT LIFE

Crump, C, Winkleby MA, Sundquist J, Sundquist K. **Preterm birth and risk of medically treated hypothyroidism in young adulthood.** Clin Endocrinol (Oxf) 2011;75:255-260.

SUMMARY

BACKGROUND

Low birth weight may be a consequence of either delayed fetal growth or preterm birth. Previous studies suggested that low birth weight is associated with thyroid autoimmunity and hypothyroidism in later life, but the potential effect of preterm birth, independent of fetal growth, is unknown. The author's objective was to determine whether preterm birth is independently associated with medically treated hypothyroidism in young adulthood. The previous studies to date were generally small and had insufficient power to examine the specific effect of preterm birth on hypothyroidism in later life. In addition, differences in effect between singletons and twins have not been previously examined. Twins are exposed to a more adverse intrauterine environment, which may potentially modify the risk of autoimmunity developing. To address these gaps in the current knowledge, the authors conducted the largest study to date to examine the potential effect of preterm birth on the risk of medically treated hypothyroidism in young adulthood.

METHODS

The authors identified 648,276 individuals in the Swedish Medical Birth Register who were born from 1973 through 1979. Of this total, the following individuals were excluded: those who were no longer living in Sweden at the time of follow-up (2005–2009); those who had congenital hypothyroidism, hypopituitarism, or significant congenital anomalies; those with missing information on birth weight; those with gestational age <23 weeks; and those with a birth weight >4 SD above or below the mean birth weight for gestational age and sex from a Swedish reference growth curve. A total of 629,806 individuals (97.2% of the original cohort), between 25.5 and 37.0 years of age during the follow-up period, remained for inclusion in the study.

Medication data were obtained using a national pharmacy register maintained by the Swedish National Board of Health and Welfare. This register contains a record of each medication prescribed by a health care provider and dispensed to a patient by any outpatient or inpatient pharmacy in Sweden. The authors obtained all outpatient and inpatient prescriptions for thyroid hormone medications which include both levothyroxine and liothyronine. The outcome was defined as an average of at least one thyroid hormone prescription per year during the follow-up period. The exposure of interest was gestational age at birth, which was based on maternal report of the last menstrual period, obtained from nationwide prenatal and birth records in a national research database (Center for Primary Health Care Research, Lund University, Lund, Sweden). Gestational age at birth was categorized as 23 to 31 weeks, 32 to 36 weeks, 37 to 42 weeks (full-term), and ≥43 weeks.

RESULTS

Of the 629,806 study participants, 27,935 (4.4%) were born prematurely (<37 weeks)—2062 (0.3%) at 23 to 31 weeks and 25,873 (4.1%) at 32 to 36 weeks. Compared to individuals who were born at full-term, those who were born prematurely were more likely to be male and/or a twin, and their mothers were more likely to be either <20 or ≥35 years old at delivery, to be divorced or never married, and to have the lowest educational attainment and/or the lowest family incomes. A total of 11,159 (1.8%) individuals were prescribed at least one thyroid hormone medication per year during the follow-up period. Individuals who were born very preterm (23 to 31 weeks) had a higher prevalence of thyroid hormone prescription than those who were born full-term (P = 0.001). Among individuals born prematurely (<37 weeks), twins had a higher prevalence of thyroid hormone prescription than singletons (2.3%, vs. 1.8%; P = 0.02). Young adults who had been born

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very preterm (23 to 31 weeks) had increased relative odds ratios of thyroid hormone prescription relative to those born at full-term. Adjustment for potential confounders, with or without fetal growth, had only modest effects on the odds ratios. In the fully adjusted model, comparing all individuals born very preterm (23 to 31 weeks) to those born full-term, the odds ratio for thyroid hormone prescription was 1.70 (95% confidence interval [CI], 1.29 to 2.23). Among twins, the association appeared to be stronger than among singletons, and an increased relative odds ratio was observed across the full range of preterm gestational ages. In the fully adjusted model for twins, the odds ratios were 2.62 (95% CI, 1.30 to 5.27) and 1.44 (95% CI, 1.02 to 2.03) for those born at 23 to 31 weeks and 32 to 36 weeks, respectively, relative to full-term births.

CONCLUSIONS

This national cohort study suggests that preterm birth is associated with an increased risk of hypothyroidism that requires medical treatment in young adulthood. This association was independent of fetal growth and appeared stronger among twins than among singletons. Additional studies are needed to confirm these new findings in other populations and to elucidate the mechanisms.

COMMENTARY

The association between low birth weight and hypothyroidism later in life has been reported in series with small number of patients. An earlier study suggested an association between low birth weight and autoimmunity but not with hypothyroidism in women evaluated at 60 to 71 years of age (1). Association with hypothyroidism has also been reported (2). The association between twin pregnancies suggested that in monozygous twin pairs with discordant birth weights, the smaller twin had a higher prevalence of thyroid peroxidase antibodies (3). However, other studies failed to confirm previous findings (4, 5). No studies specifically related to prematurity were available until the present one from Sweden. In the present study, no information was available on maternal thyroid disease during pregnancy; the only information was related to thyroid hormone prescription during the follow-up period. It could be speculated that thyroid autoimmunity was already present in many of the mothers of the patients included in the study by Crump et al., perhaps undiagnosed at the time of their pregnancies. Some of them might have had treated hypothyroidism, but the thyroxine dose was not properly adjusted during their pregnancy. Most of the patients reported were born before the need for an increased dose of thyroid hormone during pregnancy was recognized. The finding in twin pregnancy is fascinating and deserves further study, since twin studies have reported a strong genetic influence on autoimmune thyroid disease (6).

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