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Original Research

Neonatal thyroid-stimulating hormone level is influenced by neonatal, maternal, and pregnancy factors

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ABSTRACT

The percentage of newborns with a neonatal whole blood thyroid-stimulating hormone (TSH) greater than 5 mIU/L has been used as an indicator of iodine deficiency at the population level. However, TSH levels in newborns may be influenced by many factors other than iodine status. The objective of this study was to identify neonatal, maternal, and pregnancy-related determinants of neonatal TSH levels in a retrospective cohort study. The study sample included 313 Belgian mothers and their 4- to 5-year-old children. The children had a neonatal TSH concentration between 0 and 15 mIU/L at neonatal screening, and blood samples were collected 3 to 5 days after birth. Children with suspected congenital hypothyroidism (neonatal TSH level >15 mIU/L), prematurely born (ie, <37 weeks), or with a low birth weight (ie, <2500 g) were excluded. Information about maternal and birth-related determinants was collected from the neonatal screening center via a self-administered questionnaire filled in by the mother together with the child's health booklet. Higher TSH levels were found in spring and winter compared to summer and autumn ($P = .011$). Higher TSH levels were associated with lifetime smoking behavior (up to child birth) in the mother ($P = .005$), lower weight gain during pregnancy ($P = .014$), and longer pregnancies ($P = .003$). This study showed that several neonatal, maternal, and pregnancy-related determinants are influencing neonatal TSH level.

1. Introduction

Iodine is essential for the production of thyroid hormones that are necessary for the optimal development of the body and the brain [1]. Iodine deficiency during pregnancy is associated with adverse consequences such as risk of goiter, miscarriage, stillbirth, and congenital abnormalities such as cretinism [2-5]. Even at mild to moderate levels, iodine

Abbreviations: IQR, interquartile range; MID, mild iodine deficiency; TSH, thyroid-stimulating hormone; ULB, Université Libre de Bruxelles.

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deficiency may affect offspring neurodevelopment [6]. Regular monitoring of the iodine status of the population is needed because iodine deficiency can easily reappear with changes in food industry practices or nutritional habits. Besides median urinary iodine excretion in a representative sample of school-aged children and pregnant women, thyroid size, serum thyroglobulin concentration, and neonatal thyroid-stimulating hormone (TSH) concentration have been proposed as indicators of population iodine status [7-10]. Neonatal TSH concentration could indicate the iodine status of pregnant women during late pregnancy because the neonatal thyroid is very sensitive to variations of maternal iodine intake [7,11]. Neonatal thyroid iodine content is relatively low, which explains why, in the case of maternal iodine deficiency, neonatal TSH secretion increases to enhance iodine uptake and maintain normal neonate's thyroid function. In countries that screen for congenital hypothyroidism, the surveillance of iodine status throughout the analysis of percentage of TSH neonatal screening results enables regular monitoring at no extra cost. The percentage of neonatal TSH concentration greater than 5 mIU/L indicates the iodine status of a population as follow: a frequency less than 3% indicates iodine sufficiency, a frequency of 3% to 19.9% indicates mild iodine deficiency (MID), a frequency of 20% to 39.9% indicates moderate iodine deficiency, and a frequency greater than 40% indicates severe iodine deficiency [7,8,12]. However, the cutoff of 5 mIU/L has been criticized because, in some studies, the percentage of TSH results greater than 5 mIU/L was less than 3%, although other indicators of iodine status showed that this population had MID [12,13]. The cutoff of 3% of TSH screening greater than 5 mIU/L was not sensitive enough to detect MID in those studies. That may be explained by covariates affecting TSH screening results. Indeed, previous literature showed that several factors may affect TSH concentration [12,14-34], including maternal thyroid diseases and drugs, type of delivery, and birth conditions as well as methods and timing of TSH determination (see Table 1 for a summary of those factors). Without studying confounding factors, it may be difficult to establish the magnitude of iodine deficiency on neonatal TSH concentration, particularly if iodine deficiency is mild.

We hypothesized that several factors may influence neonatal TSH concentration. The aim of this retrospective cohort study is to investigate the maternal and neonatal determinants of neonatal TSH concentration measured between 3 and 5 days after birth in Belgium, a mildly iodine-deficient country.

2. Methods and materials

We used data from the PsychoTSH study, a Belgian retrospective cohort study of a sample of 313 children aged 4 to 5 years old with a neonatal TSH concentration in the range of 0 to 15 mIU/L [35]. Neonatal TSH data were obtained from the Brussels newborn screening center for metabolic disorders (Laboratoire de Pédiatrie, Université Libre de Bruxelles [ULB], Brussels). Children were selected from a total sample of 29013, 29602, and 30126 neonates screened in 2008, 2009, and 2010, respectively.

Table 1 – Factors influencing neonatal TSH level

Factors influencing neonatal TSH level
Sex [a]
Exposure of the fetus to:
Iodine excess
Iodine-containing drugs [a]
Contrast agents
Environmental contaminants
Lithium [a]
TSH receptor blocking antibodies from mothers with autoimmune thyroid disease [a]
Antithyroid drugs [a]
Maternal smoking behavior [a]
Exposure of the newborn during neonatal period to:
Iodine-containing antiseptics
Perinatal anoxia [a]
Multiple birth [a]
Pregnancy duration [a]
Low weight at birth [a]
Surgical hypothermia [a]
Type of delivery [a]
TSH testing condition
No. of days between birth and testing [a]
Season of birth [a]
TSH assay used

[a] Factors evaluated in this study.

The sample was stratified by sex and by TSH level using a stratified sampling methodology to ensure that the whole range of neonatal TSH values was represented. Children were sorted by birth years, sex, and TSH level. For each sex and TSH interval (0-1, 1-2, 2-3, 3-4, 4-5, 5-6, 6-7, 7-8, 8-9, and 9-15 mU/L), 19 newborns were randomly selected after excluding infants with possible congenital hypothyroidism (TSH, >15 mU/L) and premature and/or low-birth-weight infants (pregnancy duration <37 weeks and/or birth weight <2500 g). The day of TSH measurement was taken into account to obtain an equal distribution between days 3, 4, and 5 of life. For each newborn selected, 3 newborns with the same characteristics (sex and TSH level) were selected to be contacted in case of refusal or a noncontactable case.

Thyroid-stimulating hormone levels were measured in dried blood spots on filter paper collected 3 to 5 days after birth using a time-resolved fluoroimmunoassay (Autodelfia method) [36]. The reproducibility of the TSH values within the range of 0 to 15 mIU/L was tested. Thyroid-stimulating hormone was reanalyzed twice for 50 different TSH values to determine the coefficient of variation. It was found that, for the TSH values ranging from 0.9 to 10 mIU/L, the coefficient of variation was less than 20%. For values less than 0.9 mIU/L, a TSH value of 0.45 mIU/L was set in the study.

Date of birth, date of blood sampling, pregnancy duration, and body weight at birth were provided by the Brussels newborn screening center for metabolic disorders (Laboratoire de Pédiatrie, ULB, Brussels, Belgium).

To collect additional information about pregnancy and delivery, a home visit was organized. Data were obtained from the health booklet of the child and from a self-administered questionnaire filled in by the mother. The following information was collected: exposure of the fetus to thyroid disease of the mother, drug intake, chronic disease,