Hypothyroidism prevalence following exposure to radioiodines in childhood and adolescence: Belarusian-American Cohort Study of Thyroid Cancer and Other Thyroid Diseases after the Chernobyl Accident

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Background. Hypothyroidism is the most common thyroid abnormality in patients treated with high doses of iodine-131 (^{131}I). Data on risk of hypothyroidism from low to moderate ^{131}I thyroid doses are limited and inconsistent.

Objective. To assess the risk of hypothyroidism prevalence in relation to ^{131}I doses from Chernobyl fallout exposure.

Materials and methods. The analysis is based on the first screening cycle (1996–2003) of a Belarus-American study of thyroid diseases in a cohort of 10,827 individuals under 18 years of age at the time of the accident, with individual thyroid radioactivity measurements taken within 2 months of the accident. Screening procedures included a clinical examination and thyroid palpation by an endocrinologist and an independent thyroid palpation and ultrasonographic examination by an ultrasonographer, as well as collection of serum and spot urine samples. A series of structured questionnaires containing demographic, medical and dosimetry related questions were administered by study personnel. Thyroid-stimulating hormone (TSH), free thyroxine (FT4), and antibodies to thyroid peroxidase (ATPO) and thyroglobulin (ATG) were measured in serum and iodine in urine.

Thyroid individual doses were estimated based on 1) direct thyroid measurements, 2) radioecological model of temporal variation of ^{131}I activity in the thyroid gland and 3) data on individual dietary and lifestyle habits from personal interview. ^{131}I represents about 95% of the thyroid dose.

To assess the association of hypothyroidism prevalence with various risk factors we estimated odds ratios (ORs) and computed corresponding 95% confidence intervals (CIs) based on logistic regression analysis using the GMBO module of Epicure statistical software. We also evaluated TSH as a continuous outcome. In addition to ^{131}I thyroid dose, our analyses considered effects of sex, age at examination, place of residency, rural/ urban status, smoking, vitamin consumption, thyroid disease history in relatives, year and season of examination, level of urinary iodine, thyroid volume, ATPO and ATG levels. We fitted a linear dose-response model and evaluated departure from linearity fitting linear-quadratic and linear-quadratic-cubic dose-response models. To evaluate interaction we allowed a dose-response trend to vary within categories of different factors such as sex, age at exposure and examination, place of residency, ATPO and ATG level, urinary iodine level, smoking status, thyroid history in relatives, year of examination and rural/ urban status. Statistical significance of model parameters, test of trend and comparison in goodness of fit between the models were performed using likelihood ratio chi-square test with degrees of freedom equal to the difference in number of parameters in compared models. All statistical tests were two-sided and $p<0.05$ was considered significant.

Results. The study subjects were 50% females. Mean age at examination was 21.6 years (range, 10.9–33.4 years). 62% of the study individuals were 10 years or younger at the time of the accident. The majority of them were residents of Gomel (60% of the study subjects) and Minsk (29%) regions. Mean ^{131}I thyroid dose was 540 mGy (range, 0.8–26,639 mGy). There were 319 (2.9%) hypothyroidism cases, as defined by serum TSH level > 4 mIU/L, and 18 (0.2%) cases of overt hypothyroidism (TSH > 4 mIU/L and FT4 < 10 pmol/L).

After adjustment for thyroid dose and non-radiation risk factors, baseline hypothyroidism prevalence was significantly higher in residents of Gomel (OR=1.5; 95%CI: 1.1; 2.0) and Mogilev (OR=1.7; 95%CI: 1.1; 2.6) regions compared with residents of Minsk region; among the ATPO positive (OR=3.9; 95%CI: 2.7; 5.5) and ATG positive (OR=2.4; 95%CI: 1.6; 3.5) compared with antibody negative subjects; in subjects with low (<20 µg/L) urinary iodine level (OR = 1.5; 95%CI: 1.1; 2.2) compared with those having level of 50-99 µg/L. Rural residents had higher prevalence (OR=1.24; 95%CI: 1.0; 1.6) compared with urban residents. Smokers had reduced risk of hypothyroidism (OR=0.5; 95%CI: 0.4; 0.7) compared with non-smokers. There was a significant interaction between sex and age at examination (p = 0.02) with gradual decrease in risk with increasing age that was more pronounced in males than in females. Hypothyroidism risk decreased by 4% (95%CI: 1%; 7%) per 1 ml increase in thyroid volume (p< 0.001). Individuals examined in 1999 (OR= 0.6; 95%CI: 0.4; 0.9) and 2000-03 (OR=0.9; 95%CI: 0.7; 1.3) had a lower risk compared with those examined in the earlier years (1996-98). We found no evidence that baseline hypothyroidism risk varies with season of examination (p=0.23), vitamin consumption (p=0.62) or thyroid disease history in relatives (p=0.16).

We found a significant association between ^{131}I thyroid doses and hypothyroidism prevalence, with the excess odds ratio per gray (EOR/ Gy) of 0.33 (95% CI: 0.15; 0.60) over entire dose range. A linear-quadratic model provided a better fit compared with a simple linear model (p < 0.029); EOR estimates for linear and quadratic terms were 0.02 (95%CI: -0.24; 0.37) and 0.04 (95%CI: 0.004; 0.09), respectively. Exclusion of 18 overt hypothyroidism cases did not affect the above results. A significant linear dose-response relationship persisted after excluding subjects with doses ≥ 10Gy (n=23), although this was no longer significant after all subjects with dose ≥ 5 Gy (n=97) were excluded. Radiation-associated risk (EOR/ Gy) decreased both with increasing age at exposure (p=0.01) and at examination (p=0.03). Radiation risk was more pronounced in subjects residing in rural areas (EOR/ Gy=0.55 *vs.* EOR/Gy=0.08 in urban residents, p=0.03). EOR/ Gy was higher in ATPO negative (EOR/ Gy=0.37; 95%CI: 0.17; 0.69) compared with ATPO positive subjects (EOR/ Gy= -0.19; 95%CI:-0.38; 0.39), although not significantly different (p=0.06). Similar patterns of radiation risk were shown using TSH as a continuous outcome.

Conclusions. Our findings are in agreement with those from our previous study carried out in Ukraine, where a significant relationship was found between prevalence of hypothyroidism and ^{131}I thyroid doses from Chernobyl fallout. The radiation-related increase in hypothyroidism in Belarus was 33% per Gy and limited largely to antibody-negative hypothyroidism. Risk of radiation-associated hypothyroidism was modified by age at exposure and age at examination with the highest risk found among younger individuals. Prospective data are needed to evaluate the dynamics of radiation-related hypothyroidism.