

# Fluoride exposure and hypothyroidism in a Canadian pregnancy cohort





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## Introduction & Objective

- Maternal thyroid hormones during pregnancy are critical for optimal fetal growth and development.<sup>1,2</sup>
- Fluoride has been associated with thyroid dysfunction, including hypothyroidism, at low and high levels of exposure.<sup>3-6</sup>
- Little is known about the risk of hypothyroidism among pregnant women exposed to fluoride.

#### **Objective:**

 To investigate the association of fluoride exposure and hypothyroidism in a cohort of pregnant women in Canada.

### Methods

Participants: 1436 pregnant women enrolled (recruited between 2008 and 2011) in the Maternal-Infant Research on Environmental Chemicals (MIREC) cohort study.

#### Three fluoride exposure variables:

- 1. Water fluoride concentration measured in municipal drinking water (mg/L).
- 2. Fluoride intake estimated from self-reported beverage consumption (mg/day).
- 3. Maternal urinary fluoride concentration standardized for specific gravity (mg/L).

Diagnosis of Hypothyroidism (yes/no): Women who reported a diagnosis of clinical hypothyroidism or taking medication to treat it vs. euthyroid controls.

Analyses: Logistic regression to quantify risk of self-reported diagnosis of hypothyroidism. All models were adjusted for maternal age, pre-pregnancy body mass index, level of education, race, and city of residence.

#### Table 1. Fluoride Exposure and Women's Thyroid Status.

Fluoride exposure	Median (IQR)		
Water fluoride concentration (mg/L)	0.52 (0.49)		
Fluoride intake (mg/day)	0.61 (0.74)		
Maternal urinary fluoride (mg/L)	0.50 (0.42)		
	Diagnosis of Hypothyroidism		
	Yes	No	
n (%)	58 (4.04)	1378 (95.96)	
TSH (µIU/mL; M±SD)	1.65 (±1.04)*	1.28 (±0.76)	
Total T4 (ng/mL; M±SD)	118.66 (±25.23)*	105.96 (±20.97)	
Anti-Thyroglobulin (IU/mL; median(IQR))	7.40 (25.88)*	1.10 (1.82)	
Anti-Thyroperoxidase (IU/mL; median(IQR))	41.44 (277.21)*	0.42 (0.55)	
*p < .001, two-tailed.			

### Results

- A 0.5 mg/L increase in water fluoride concentration was associated with a two-fold increased odds of having hypothyroidism. Thus, Table 2. Odds of Hypothyroidism Diagnosis Predicted by Water Fluoride, Fluoride Intake, and MUF<sub>SG</sub>. a 0.5 mg/L increase in water fluoride implies increasing the probability of a hypothyroidism diagnosis in the general population from 2% to 4%.
- A 0.5 mg increase in fluoride intake per day was associated with a 1.5 times greater odds of having hypothyroidism, meaning that women who consumed more fluoride through their diet had a greater probability (i.e., 2.9%) of being diagnosed with hypothyroidism.
- There was no significant association between maternal urinary fluoride concentration and hypothyroidism.

#### Sensitivity analysis:

For women who reported living at their current residences for at least one year, water fluoride concentration was associated with an even greater odds of having hypothyroidism (OR for 0.5 mg/L increase = 2.27; 95% CI: 1.19, 4.35; p = .013; probability = 4.4%).

### Click tables to enlarge

Fluoride exposure	n	Adjusted OR	95% CI	p
Water fluoride	1260	2.05 <sup>a</sup>	1.15, 3.66	.014
Fluoride intake	1116	1.46 <sup>b</sup>	1.08, 1.97	.014
Maternal urinary fluoride	1436	0.97 <sup>a</sup>	0.67, 1.40	.864

<sup>a</sup>ORs for water fluoride, and maternal urinary fluoride reported for every 0.5 mg/L increase in fluoride concentration. This represents the difference in exposure between women living in a fluoridated community vs. those living in a non-fluoridated community.

<sup>b</sup>OR for fluoride intake reported for every 0.5 mg increase in fluoride intake per day, which represents the approximate difference in dietary fluoride consumption between women at the 25th percentile and the 60<sup>th</sup> percentile of fluoride intake.

### Conclusions

- Women living in communities with fluoridated tap water had a higher risk of hypothyroidism in this Canadian pregnancy cohort.
- Fluoride in drinking water, but not maternal urinary fluoride, was significantly associated with risk of hypothyroidism. Water fluoride concentration may be more indicative of chronic fluoride exposure than urinary fluoride; urinary fluoride is more indicative of current exposure levels.
- Further research is needed to understand how fluoride exposure may disrupt thyroid function in pregnancy and whether alterations to thyroid hormones may mediate neurobehavioral outcomes in offspring.

### References

#### For full reference list or more information, please email: mkhall@yorku.ca

- 1. De Escobar, G. M., Obregón, M. J. & Del Rey, F. E. Role of thyroid hormone during early brain development. European Journal of Endocrinology 151, U25–37 (2004). 2. Thompson, W. et al. Maternal thyroid hormone insufficiency during pregnancy and risk of neurodevelopmental disorders in offspring: A systematic review and meta
  - analysis. Clinical Endocrinology (Oxf). 88, 575-584 (2018). 3. Khandare, A. L., Validandi, V., Gourineni, S. R., Gopalan, V. & Nagalla, B. Dose-dependent effect of fluoride on clinical and subclinical indices of fluorosis in school going
  - children and its mitigation by supply of safe drinking water for 5 years: an Indian study. Environmental Monitoring and Assessment 190, 110 (2018). 4. KheradPisheh, Z. et al. Impact of drinking water fluoride on human thyroid hormones: A case-control study. Scientific Reports 8, 1–7 (2018).
- 5. Chaitanya, N. et al. A systematic analysis on possibility of water fluoridation causing hypothyroidism. Indian Journal of Dental Research 29, 358–363 (2018). 6. Peckham, S., Lowery, D., & Spencer, S. Are fluoride levels in drinking water associated with hypothyroidism prevalence in England? A large observational study of GP practice data and fluoride levels in drinking water. Journal of Epidemiology and Community Health 69, 619-624 (2015).

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Table 2. Odds of Hypothyroidism Diagnosis Predicted by Water Fluoride, Fluoride Intake, and MUF<sub>SG</sub>.

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Fluoride exposure has been associated with thyroid dysfunction, but little is known about the risk of hypothyroidism among pregnant women exposed to fluoride. We investigated the association between fluoride exposure and hypothyroidism in Canadian pregnant women enrolled in the Maternal-Infant Research on Environmental Chemicals cohort study. Using a case-control design. we compared pregnant women who reported a diagnosis of clinical hypothyroidism or reported taking medication to treat hypothyroidism (n=64) against nonhypothyroid controls. We measured fluoride concentration in drinking water (n=1260) and in urine averaged across three trimesters and standardized for specific gravity (n=1436). We also estimated prenatal fluoride intake based on self-reported beverage consumption (water, coffee, tea) (n=1116). We assessed the association between fluoride exposure and hypothyroid status using logistic regression models adjusted for maternal age, prepregnancy body mass index, level of education, race, and city of residence. The median  $\pm$  SD water fluoride concentration and fluoride intake level was 0.52  $\pm$  0.26 mg/L and 0.61  $\pm$  0.54 mg/day; the median urinary fluoride concentration was 0.50  $\pm$  0.39 mg/L. A 0.5 mg/L increase in water fluoride concentration was associated with a 2.05 (95%CI: 1.15, 3.66) increased odds of having hypothyroidism. Similarly, a 0.5 mg increase in fluoride intake per day was associated with a 1.46 (95%CI: 1.08, 1.97) increased odds of having hypothyroidism. In contrast, we observed no significant association between urinary fluoride concentration and hypothyroidism (OR for 0.5 mg/L increase=0.97; 95%CI: 0.67, 1.40). Higher exposure to fluoride from drinking water was most strongly associated with higher risk of hypothyroidism in pregnant women, suggesting that chronic fluoride exposure may be more strongly associated with hypothyroidism than contemporaneous measures, such as urinary fluoride.