ASSOCIATION OF TYPE 1 DIABETES MELLITUS AND DRINKING WATER CONTAMINATION IN NL

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The Association of Type 1 Diabetes Mellitus and Drinking Water Contamination in Newfoundland and Labrador

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Table of Contents

Executive Summary

NL has reported one of the highest incidences of childhood Type 1 diabetes mellitus (T1DM) worldwide and the rates are increasing. Although genetic susceptibility is necessary for the development of T1DM, the etiology of this disease is multifactorial and includes both genetic and environmental influences. Drinking water quality – including nutrients, metals, physical parameters and major ion concentrations - has been identified as a potential risk factor for T1DM in other regions. Using tap-water quality data for public water (Water Resources Management Division of the NL Department of Environment and Conservation) and T1DM incidence data from the NL Pediatric Diabetes Database, we analyzed potential relationships between specific water quality indicators and T1DM at the community and regional level. Our data has shown that arsenic; fluoride, copper and uranium were associated with higher rates of T1DM. Minerals such as nickel and barium were negatively associated with rates of T1DM. However to confirm these results, further detailed studies are required.

I. Introduction and Project Background

The incidence of childhood T1DM is steadily increasing in many parts of the world including NL. NL has reported the highest incidence of childhood T1DM in North America and the third highest worldwide. Although genetic susceptibility is necessary for the development of T1DM, the etiology of this disease is multifactorial and includes both genetic and environmental influences. Evidence derived from research in this area including the rising rates of the disease points toward an increased effect of environmental factors which trigger the onset and development of the disease.

II. Rationale

As rates of T1DM are increasing an understanding of proposed environmental risk factors is crucial. Drinking water quality – including nutrients, metals, physical parameters and major ion concentrations - has been identified as a potential risk factor for T1DM in other regions. Given that Newfoundland has one of the highest rates of childhood T1DM in the world and good data about water quality, it is an excellent environment to test this hypothesis.

III. Objectives

To determine the relationship between various components of drinking water and the development of T1DM in children aged 0-15 years in NL. The study examined the null hypothesis that drinking water quality has no effect on the development of T1DM later in life. The alternative hypothesis states that some components of drinking water are associated with later childhood T1DM development among children aged 0-15 years in NL.

IV. Research Methodology and Approach

4i Water Quality Data

The Water Resources Management Division of the NL Department of Environment and Conservation has systematically collected and analyzed tap-water quality data for public water supplies since 2001. This data is readily available through the government website. Using all reliable data available at the time of analysis, our study period was limited to between 2001-2012. The indicators used for analyses in this study are summarized in Table I. Data for each community was averaged over the sampling period to produce one representative value for each indicator. The census subdivision (CS) and larger census

consolidated subdivision (CCS) units were determined for each community as per Statistics Canada designations.

4ii T1DM Case Data

The number of new cases of T1DM in the province for each year between 2001-2012 (corresponding to available water quality data) was determined using data from the NL Pediatric Diabetes Database. This database includes all cases of T1DM aged 0-14 years diagnosed in the province from 1987 to present. Patient sex, month of onset of diabetes, month of birth, age of onset and community are collected and recorded by diabetes nurse educators in each facility that cares for children with T1DM and reports of new cases are faxed to the research nurse monthly at the Janeway Pediatric Research Unit at the tertiary care Janeway Children's Health and Rehabilitation Centre, Eastern Health, in St. John's. Classification, case definition and ascertainment are described elsewhere [1, 2]. Ascertainment using this method was found to be 97%.

4iii Community (CS) Incidence

Average T1DM incidence rates (number of new cases per year/100,000 children aged 0-14 years) were determined for each community (CS) using the number of new cases per year divided by the average population of children aged 0-14 during the study period (using data from the 2006 and 2011 Canadian census; Stats Canada)

4iv Regional (CCS) Incidence

Regional (CCS) T1DM rates (number of new cases per year/100,000 children aged 0-14 years) were also determined by aggregating the community incidences within each of the 89 CCS represented. Note that for the purpose of this study, these incidences are among children living in communities serviced by public water supplies within each region, rather than the total incidence for the region.

4v Inclusion/Exclusion Criteria

T1DM cases occurring in communities not supplied by public water were excluded from the analyses. Water quality data for a total of 398 municipalities were available through the provincial database. Ten of those municipalities listed multiple sources that could be attributed to 23 different communities, while 33 communities were excluded for having insufficient data (less than 12 water quality measurements during the study period), resulting in a total of 378 communities available for preliminary and regional-level analyses. Community-level population data was not available for 138 communities (in those cases, data was available only for standard geographic units containing multiple

communities). As a result, 240 communities were available for community-level analyses.

4vi Statistical Analyses

Statistical analyses were carried out using SPSS (v 22). Using a one-way ANOVA water quality indicator data for communities with at least one case of type 1 diabetes were compared to those of communities that had no cases of T1DM. Linear regression analysis was used to assess potential relationships between specific water quality indicators and T1DM at the community level (using the 240 communities with specific population data available). Recognizing the issues around analyzing incidence in small communities, regression analyses were also carried out at a regional level using regional T1DM incidence determined above and water quality data aggregated according to CCS. Prior to aggregation, water quality indicators were weighted according to the proportion of regional population serviced.

V. Clearances

The Newfoundland and Labrador Heath Research Ethics Board approved this study.

VI. Results

6i T1DM Incidence

The NL Pediatric Diabetes Database contained 499 cases in 159 communities during the study period between 2001-2012. Based on an average population of 80,403 children aged 0-14, an incident rate of 51.7/100,000 was determined for the province during the study period.

Of those cases, 434 (87%) occurred in 114 communities serviced by public water supplies, while the remaining 264 communities reported no cases of T1DM during the study period. Among the 240 communities with population data, a total of 409 cases (in 95 communities) result in an incident rate 51.2/100,000 during the study period. The individual incidence rates in those communities (many of which have small populations) reporting at least one case of T1DM during the study period averaged 154.1/100,000 (± 175.2 SD) and ranged from 16.2 to 1282.1/1000,000. All 378 communities with sufficient water quality data were included in regional level analyses. Regional incidence rates for each CCS averaged 47.4/100,000 (± 54.3 SD) and ranged from 0 to 267.6/100,000.

6ii Community-Level Analyses

Comparison of water quality indicator levels between communities reporting cases of T1DM during the study period and those reporting no cases indicated significant differences in ammonia, barium, copper, lead, magnesium, uranium, calcium and chloride concentrations (Table 1). Linear regression analysis using concentrations of minerals and elements indicated that arsenic concentration (ß = 0.27, p=0.013) was positively associated with type 1 diabetes incidence rate. Two other indicators, copper (ß = -0.16, p = 0.06) and uranium (ß = -0.23, p = 0.06), approached significance and overall model fit was R2 = 0.09. Analysis of major ions indicated that fluoride level (ß = 0.20, $p < 0.05$) was positively associated with T1DM incidence rate. Overall model fit was R2 = 0.10 (Table 2).

6iii Regional-Level Analyses

Regression analysis of concentrations of minerals and elements indicated that barium (ß = -0.48, $p < 0.05$) and nickel levels (ß = -0.35, p = 0.05) were negatively associated with T1DM incidence rate. Overall model fit was R2 = 0.21. Analysis of major ions did not indicate any significant associations (Table 1).

6iv Recommendations on Public Policy

The results from this research should be considered preliminary data which require further research to confirm or refute our findings. As T1DM rates in NL are amongst the highest in the world more research should be conducted examining the contribution of potential environmental risk factors of this disease. The unique population of NL proves useful as rates of childhood T1DM vary with geographical location thus allowing for comparison within the province. Study results will be made available to different stakeholders in NL, such as clinicians, the research community as well as government and will provide a foundation for future research regarding potential environmental risk factors of childhood T1DM in NL.

VII. Conclusions

Our data has shown that higher concentrations of arsenic and fluoride in drinking water may be associated with an increase incidence of T1DM as well as metals such as copper and uranium. Minerals such as nickel and barium may be associated with a decreased incidence of T1DM. However to confirm these results, further detailed studies are required.

VIII. References

Alaghehbandan, R., Collins, K. D., Newhook L. A., MacDonald, D., 2006 Childhood type 1 diabetes mellitus in Newfoundland and Labrador, Canada. *Diabetes Research and Clinical Practice*, 74:1, 82-89.

Bear, J. C., Kennedy, J. C., Marshall, W., Power, A. A., Kolonel, V. M., Burke, G. B., 1987 Persistent genetic isolation in outport Newfoundland. *American Journal of Medical Genetics*, 27: 807-30.

Casu, A., Carlini, M., Contu, A., Bottazzo, G. F., Songini, M., 2000 Type 1 diabetes in Sardinia is not linked to nitrate levels in drinking water. *Diabetes Care*, 23 (7): 1043-44.

DIAMOND Project Group, 2006: Incidence and trends of childhood Type 1 diabetes worldwide 1990-1999. *Diabetic Medicine*, 23 (8): 857-66.

Gale, E. A. M., 2002 The rise of childhood Type 1 diabetes in the 20th century. *Diabetes*, 51 (12): 3353-61.

Haglund, B., Ryckenberg, K., Selinus, O., Dahlquist, G., 1996 Evidence of a relationship between childhood-onset type 1 diabetes and low groundwater concentration of zinc. *Diabetes Care*, 19 (8): 873-5.

International Diabetes Federation, IDF Diabetes Atlas, 5th edn, Brussels, Belgium: International Diabetes Federation, 2011. http://idf.org/diabetesatlas

International Diabetes Federation, IDF Diabetes Atlas, 5th edn, 2012 Update. Brussels, Belgium: International Diabetes Federation, 2012. http://www.idf.org/diabetesatlas/5e/Update2012

Kostraba, J. N., Gay, E. C., Rewers, M., Hamman, R. F., 1992 Nitrate levels in community drinking waters and risk of IDDM: An ecological analysis. *Diabetes Care*; 15 (11): 1505-8.

Muntoni, S., Cocco, P., Muntoni, S., Aru., G., 2006 Nitrate in community water supplies and risk of childhood type 1 diabetes in Sardinia, Italy. *European Journal of Epidemiology;* 21: 245-7.

Newhook, L. A., Grant. M., Sloka, S., Hoque, M., Paterson, A. D., Hagerty, D., Curtis, J., 2008. Very high and increasing incidence of type 1 diabetes mellitus in Newfoundland and Labrador, Canada. *Pediatric Diabetes*, 9: (3 Pt 2): 62-8.

Newhook, L. A., Penney, S., Fiander, J., Dowden, J., 2012. Recent incidence of type 1 diabetes mellitus in children 0-14 years in Newfoundland and Labrador, Canada climbs to over 45/100 000: a retrospective time trend study.

Parslow, R. C., McKinney, P. A., Law, G. R., Staines, A., Williams, R. Bodansky, H. J., 1997. Incidence of childhood diabetes mellitus in Yorkshire, northern England, is associates with nitrate in drinking water: an ecological analysis. *Diabetologia;* 40: 550-6.

Public Health Agency of Canada, 2011, Diabetes in Canada: Facts and figures from a public health perspective. Ottawa, Canada. http://www.phac-aspc.gc.ca/cd-mc/publications/diabetes-diabete/facts-figures-faits-chiffres-2011/index-eng.php#toc

Rahman, M., Tondel, M., Ahmad, S., Axelson, O., 1998. Diabetes Mellitus Associated with Arsenic Exposure in Bangladesh. *American Journal of Epidemiology*; 148 (2): 198-203.

Samuelson, U., Oikarinen, S., Hyoty, H., Ludvigsson, J., 2011 Low zinc in drinking water is associated with risk of type 1 diabetes in children. *Pediatric Diabetes*; 12: 156-64.

Stene, L. C., Hongve, D., Magnus, P., Ronningen, K. S., Joner, G., 2002. Acidic drinking water and risk of childhood-onset type 1 diabetes. *Diabetes Care*; 25 (9): 1534-8.

Van Maanen, J. M. S., Albering, H. J., Van Breda, S. G. J., Curfs, D. M. J., Ambergen, A. W., Wolffenbuttel, B., H., R., Kleinkams, J., C., S., Reeser, H., M., 1999. Nitrate in drinking water and risk of childhood diabetes in the Netherlands. *Diabetes Care,* 22 (10): 1750.

Zhao, H. X., Mold, M. D., Stenhouse, E. A., Bird, S. C., Wright, D. E., Demaine, A. G., Millward, B. A., 2001. Drinking water composition and childhood-onset Type 1 diabetes mellitus in Devon and Cornwall, England. *Diabetic Medicine*; 18: 709-17.

IX. Tables

Water Quality Indicator	Community-Level Linear Regression		Regional Level Linear Regression	
Nutrients & Metals	**Beta**	**P Value**	**Beta**	**P Value**
Ammonia	0.010	0.901	-.044	.758
DOC	-0.094	0.496	-.162	.589
Nitrate(ite)	-0.015	0.868	.319	.094
Kjeldahl Nitrogen	-0.146	0.220	.061	.825
Total Phosphorus	0.095	0.214	.047	.797
Aluminum	0.014	0.868	-.022	.875
Antimony	-0.166	0.143	.089	.525
Arsenic	0.268	0.013 *	-.173	.458
Barium	0.020	0.860	-.478	.009 *
Cadmium	0.005	0.975	1.252	.138
Chromium	0.040	0.677	.212	.524
Copper	-0.157	0.061	-.139	.502
Iron	0.159	0.137	.025	.904
Lead	0.119	0.243	-.031	.853
Magnesium	-0.031	0.719	.083	.606
Manganese	0.001	0.989	.098	.488
Mercury	0.081	0.590	-.974	.251
Nickel	0.043	0.585	-.354	.050 *
Selenium	0.007	0.963	-.021	.961
Uranium	-0.231	0.056	-.191	.328
Zinc	-0.029	0.776	-.130	.558
Major Ions				
Boron	0.216	0.109	-.176	.480
Bromide	-0.015	0.860	.038	.860
Calcium	-0.560	0.116	.046	.740
Chloride	1.255	0.082	.202	.310
Fluoride	0.202	0.005 *	.177	.325
Potassium	-0.133	0.287	-.185	.232
Sodium	-0.319	0.384	-.165	.452
Sulphate	0.964	0.076	.107	.490

Table 1. Linear regression analyses of water quality indicator levels and T1DM incidence rate at both community and regional levels.

Water Quality Indicator	One-way ANOVA Analyses		
Nutrients & Metals	**F Value**	**P Value**	**Sig**
Ammonia	7.65	0.006	*
Dissolved Organic Content	3.80	0.052	
Nitrate(ite)	1.78	0.183	
Kjeldahl Nitrogen	1.14	0.287	
Total Phosphorus	0.64	0.426	
Aluminum	0.02	0.886	
Antimony	1.62	0.204	
Arsenic	1.82	0.178	
Barium	4.57	0.033	*
Cadmium	0.22	0.637	
Chromium	0.60	0.438	
Copper	4.94	0.027	*
Iron	1.03	0.309	
Lead	4.71	0.031	*
Magnesium	6.85	0.009	*
Manganese	1.69	0.195	
Mercury	0.89	0.345	
Nickel	0.38	0.537	
Selenium	2.82	0.094	
Uranium	4.24	0.040	*
Zinc	3.16	0.076	*
Physical Parameters & Major Ions			
Alkalinity	6.43	0.012	*
Colour	9.55	0.002	*
Conductivity	7.74	0.006	*
Hardness	6.78	0.010	*
pH	1.73	0.189	
TDS	7.61	0.006	*
TSS	1.20	0.275	
Turbidity	4.07	0.044	*
Boron	0.63	0.428	
Bromide	1.30	0.255	
Calcium	5.86	0.016	*
Chloride	4.26	0.040	*
Fluoride	0.52	0.470	
Potassium	4.35	0.038	*
Sodium	4.63	0.032	*
Sulphate	0.64	0.425	

Table 2. Comparison of water quality indicator levels between communities reporting cases of T1DM during the study period and those reporting none (One-way ANOVA; significant difference defined as $p < 0.05$)