Original article

The association of type 2 diabetes and insulin resistance/secrection with persistent organic pollutants in two First Nations communities in northern Ontario

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Abstract

\textbf{Aims.} – Recent evidence suggests an association between persistent organic pollutants (POPs) and type 2 diabetes. In two First Nations communities where wild food is consumed by a large portion of the population, we compared pollutants in plasma between diabetic and non-diabetic individuals, and investigated the strength of association between pollutants and insulin resistance/secrection in non-diabetic individuals.

\textbf{Methods.} – The study population consisted of 72 participants. Oral Glucose Tolerance Tests were used to assess diabetes status. Plasma was used to determine POP concentrations and mercury concentrations were determined from hair samples.

\textbf{Results.} – Age-adjusted plasma concentrations of some pollutants were significantly higher in diabetic than in non-diabetic individuals. When taking into account age, adiposity levels, and smoking status, POP levels were not associated with insulin resistance nor with insulin secretion in non-diabetic individuals.

\textbf{Conclusions.} – These findings confirm that POP concentrations in plasma may be higher in diabetic than in non-diabetic individuals. No association was however seen between POP concentrations and markers of insulin resistance/secrection in non-diabetic individuals.

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Keywords: Persistent organic pollutants; Diabetes; Insulin resistance; Inflammation; First Nation

Résumé

Un lien entre les polluants organiques persistants et le diabète de type 2 au sein de deux communautés de Premières Nations du nord de l’Ontario.

\textbf{Buts.} – De récentes évidences suggèrent un lien entre les polluants organiques persistants (POPs) et le diabète de type 2. Au sein de deux communautés de Premières Nations à l’intérieur desquelles une portion importante de la population consomme de la nourriture traditionnelle, nous avons : comparé les concentrations plasmatiques de polluants entre les diabétiques et les non-diabétiques ; investigué la force de l’association entre les polluants et la résistance à l’insuline et la sécrétion d’insuline chez les non-diabétiques.

\textbf{Méthodes.} – Cette étude se composait de 72 individus. Les participants ont réalisé un test de tolérance au glucose. Les concentrations plasmatiques de POP et les concentrations de mercure à partir du cuir chevelu ont été effectuées.

\textbf{Résultats.} – Les concentrations plasmatiques de certains polluants étaient significativement plus élevées chez les diabétiques en comparaison aux non-diabétiques. Lorsque l’âge, le niveau d’adiposité et le statut de fumeur sont pris en considération, les concentrations de POP n’étaient pas associées à l’insulino-résistance ou la sécrétion d’insuline chez les non-diabétiques.

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1. Introduction

In Canadian First Nations communities, the prevalence of type 2 diabetes has been reported to be 3 to 5 times higher than the general Canadian population [1]. The biological predispositions and potential environmental factors that contribute to this high rate of type 2 diabetes in Canadian Aboriginal populations were recently reviewed by Haman et al. [2] and include an elevated incidence of obesity [3], low physical activity [4], and poor availability of nutritious foods [5].

Recent evidence indicates a possible association of the development of type 2 diabetes with persistent organic pollutants such as polychlorinated biphenyls (PCBs [6–8]), organochlorine pesticides [6,7,9], and most recently polybrominated diphenyl ethers (PBDEs) [10]. Mercury has been found to be a potential risk factor for the development of insulin resistance [11]. There is also evidence for the contribution of PCBs and pesticides to the development of insulin resistance [12].

Organic pollutants are semi-volatile and can travel to remote areas through the atmosphere [13]. These pollutants do not degrade easily in the environment and can therefore bioconcentrate into organisms and biomagnify through food chains. These contaminants pose a risk to individuals consuming country foods [14]. First Nations communities traditionally rely on many foods derived from the land and could potentially be exposed to higher levels of pollutants than the general population.

Given the apparent association between POPs and type 2 diabetes, there is a potential for these pollutants to lead to the development of the disease. Type 2 diabetes is caused by the body’s gradual development of insulin resistance and pancreatic β-cell dysfunction. Insulin resistance refers to a decreased sensitivity of the body to insulin; a state wherein cells are less efficient at removing glucose from the blood and are not inhibited by insulin to release glucose from the liver [15], leading to the eventual decline of insulin production. Type 2 diabetes and insulin resistance are related to low-grade chronic inflammation [16], which involves similar signaling molecules as acute inflammation [17]. Inflammatory cytokines such as tumor necrosis factor (TNF)-α and interleukin (IL)-6 have been shown to increase resistance to insulin [18,19]. Conversely, the anti-inflammatory marker adiponectin is known to be positively related to insulin sensitivity [20]. Some research shows that the production of inflammatory markers is linked in part to the aryl hydrocarbon receptor [21]. This receptor is a ligand-activated transcription factor, which upregulates genes that control the metabolism of toxins that activate the receptor [22]. The receptor pathway can be activated by dioxins and coplanar (or dioxin-like) PCBs [23] and has been shown to lead to the production of TNF-α and IL-6 by certain pollutants on adipocyte cells in vitro [24]. Adiponectin has been inversely correlated to the non-coplanar congener PCB-153 levels in human plasma [25]. Although PCB-153 has virtually no binding affinity to the aryl hydrocarbon receptor [23], it often serves as a marker for total PCB exposure [26].

Given the increased prevalence of diabetes in First Nations communities and the potential for a high exposure to certain pollutants, our objectives were to investigate whether diabetic individuals had higher concentrations of pollutants in plasma, and to determine if any of the pollutants were correlated with insulin resistance/secretion in non-diabetic individuals.

2. Methodology

2.1. Site overview and participant recruitment

The study was a collaboration between the University of Ottawa, Shigogama First Nations Council, and Nishnawbe Aski Nation. Participants were recruited from Wapekeka and Kasabonika, which are two of the five Shigogama communities in northern Ontario. These communities are representative of numerous communities in remote boreal northern Ontario – a region of unique lifestyle and diet [27]. Recruitment procedures and community characteristics have been detailed elsewhere [3]. A total of 83 people were interviewed through the assistance of local research coordinators and translators who were hired over the course of the study.

In both communities, 72 individuals, of the 83 originally recruited, agreed to be research participants in the study. The participating individuals represented 24% and 9% of the adult population of Wapekeka and Kasabonika First Nations communities, respectively. The inclusion criteria were that a person must be Aboriginal, over 18 years of age, not pregnant, and free of type 1 diabetes. The study was approved by the University of Ottawa and Health Canada Research Ethics Boards. The participants gave their written informed consent to participate in the study. Results were shared with the Band Council and interested community members before being sent for publication. This manuscript was also reviewed by Band representatives from both communities prior to submission for publication.

2.2. Food intake

Participants were recruited based on self-described dietary behaviour as either relying predominantly on land based food items (primarily wild game) or predominantly market foods. Semi-structured interviews and participation/observation in daily food practices assisted in determining dietary behaviour of participants. A wild food index was created and each participant
was ranked (0 to 100) based on their frequency of wild food consumption. Participants given a score of 60 or higher ate more than 2 wild food meals per week. Participants with a score of 40 or lower ate less that 1 wild food meal per month.

2.3. Anthropometric measurements

From mid-September to early November of 2007, clinical sessions were conducted by two members of the research team in each of the two communities. These sessions included anthropometric measurements and Oral Glucose Tolerance Tests. Body weight was determined with a standard beam scale after removing the participant’s shoes. Height was measured with the participant’s bare feet together, with heels, back, and head against the wall, and following a normal inspiration. Waist circumference was measured directly on the skin (in duplicate, then averaged) following standard World Health Organization procedure.

2.4. Insulin and glucose measurements

Participants were asked to fast for 9 hours prior to the clinical session. All sessions were scheduled for 9:00 to 9:30 in the morning and participants were asked whether they were fasted upon arrival. Participants were also asked to refrain from any vigorous exercise 48 hours prior to the clinical session and requested not to smoke or drink anything but water after waking up before the clinical session. The 2-hour Oral Glucose Tolerance Test was performed using 75 g of glucose dissolved in 300 mL of water and 17 g of lemon juice added for taste. A baseline blood sample was taken before administration of the glucose drink and was used to establish fasting glucose and insulin levels. Post-ingestion, blood samples were taken at 15, 30, 60, and 120 minutes to determine glucose and insulin concentrations. Blood samples were taken using 6 mL evacuated, sterile blood collection EDTA tubes (BD Vacutainer, Fisher Scientific, Ottawa, Canada). Samples were immediately centrifuged at 3500 rpm and plasma was temporarily stored at −20°C in the clinic, before being shipped on ice to the laboratory where they were stored at −80°C.

Plasma glucose concentrations were assayed using spectrophotometric analysis after conversion of glucose to glucose 6-phosphate by hexokinase [28]. Laboratory-grade reagents (Sigma-Aldrich Canada Ltd., Oakville, Ont; Fisher Scientific Ltd., Nepean Ont.) were used to prepare a standard hexokinase reaction, and after incubating prepared samples at room temperature for 30 minutes, spectrophotometric analysis of resultant nicotinamide adenine dinucleotide light absorbance was performed in duplicate using a synergy HT series multidetection reader (Bio-Tek Instruments Inc., Highland Park, Winooski, Vt.), with absorbance readings of 340 nm wavelength emissions. All samples collected from each individual were analysed on the same plate, in duplicate. The intra-assay coefficient of variation for glucose analyses was 3.2 ± 2.8%. Based on World Health Organization standards, participants with a resting plasma glucose level greater than 7.0 mmol/L and/or a post-prandial level (2 hours after glucose ingestion) greater than 11.0 mmol/L were established as type 2 diabetic (n = 26). The rest of the participants were considered non-diabetic (n = 46). A 2-site enzyme-linked immunosorbent assay (ELISA) using 2 monoclonal antibodies (LINCO Research, St-Louis, Mo.) was used to measure plasma insulin levels with intra-assay coefficient of variation of 4.1 ± 3.8%.

Insulin resistance was quantified using the Homeostasis Model Assessment (HOMA-IR) [29]. The HOMA-IR values were obtained by dividing the product of the fasting plasma glucose (mmol/L) and insulin (μIU/mL) values by 22.5. Insulin secretion was also quantified using the HOMA for β-cell function, computed as the product of fasting plasma insulin and 3.33 divided by the difference between the fasting plasma glucose and 3.5 [29].

2.5. Inflammatory marker analysis

Measurements of all inflammatory markers were done using the plasma samples collected in the fasted state from participants through ELISA kits (R&D Systems Inc.). Plasma tumor necrosis factor (TNF)-α levels had an average intra-assay variability of 6.8 ± 5.8% and sensitivity of 0.106 pg/mL. Plasma interleukin-6 levels had an average intra-assay variability of 6.8 ± 5.5% and sensitivity of 0.70 pg/mL. Adiponectin had an average intra-assay variability of 1.9 ± 1.7% and sensitivity of 0.246 ng/mL.

2.6. Contaminant analysis

All POP measurements were done by the Toxicology Centre at the National Institute of Public Health of Quebec. The measured contaminants include Aroclor 1260, PCB28, PCB52, PCB99, PCB101, PCB105, PCB118, PCB128, PCB138, PCB153, PCB156, PCB163, PCB170, PCB180, PCB183, PCB187, aldrin, α-chlordane, γ-chlordane, β-HCH, cis-nonachlor, trans-nonachlor, DDE, DDT, hexachlorobenzene, mirex, oxychlordane, PBB153, PBDE47, PBDE99, PBDE100, PBDE153, Parlar26, and Parlar50. The plasma samples were enriched with internal standards and denatured with formic acid. The compounds were then extracted from the aqueous matrix using solid phase separation and extracts were cleaned using Florisil® columns prior to analysis. Plasma samples were eluted from columns using methylene chloride-hexane (25:75 vol/vol) and analyzed on an E-446 Agilent 6890 GC-MS (gas chromatograph–mass spectrometer) equipped with dual capillary columns. Peaks were identified by relative retention times obtained on the two columns using a computer program developed by the Quebec Toxicology Centre. Generated ions were measured after negative chemical ionization. The concentration of each analyte measured was determined using percent recovery of labelled internal standards. The electron capture detector (Agilent G2397A) served to verify the detection limits for PCB congeners 28 and 52. To verify results, an interlaboratory comparison was made with the External Quality Assessment Scheme (G-EQUAS), Germany. Mercury levels in hair were analyzed at the Laboratory for the analysis of natural and synthetic environmental toxins at the University of Ottawa. Hair was clipped as close as possible to the scalp and cleaned in a 2:1 chloroform:

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methanol solution once transported back to the laboratory. Total mercury levels were isolated using a mercury SP-3D analyzer (Nippon Instruments Corporation, Japan) and detected using cold vapour atomic absorption spectroscopy.

A POP was removed from further analysis if more than 40% of individuals had values below the instrument detection limit [30]. These included: aldrin, α-chlordane, γ-chlordane, DDT, Parlar26, Parlar50, PBB153, PBDE100, PBDE153, PBDE99, PCBs 28, 52, 101, and 128. For 14 of the other 20 pollutants originally measured, less than 40% of individuals had values below the detection limit. Random numbers were generated between 0 and the detection limit of these pollutants for each participant below the detection limit [31]. The replacement of non-detects with random numbers was performed to reduce statistical bias. The other six pollutants (which included oxychlordane, DDE, Aroclor1260, PCBs 138, 153, and 180) had a 100% detection frequency for participants. All POPs were adjusted according to plasma lipid content, in order to compare to other populations where POP concentrations are reported after lipid standardization. This was done by dividing the wet weight of each POP (µg/L) by the plasma lipid content (kg/L).

2.7. Statistical analyses

All statistical analyses were conducted using JMP version 5.1.2. An analysis of covariance (ANCOVA) was used to compare contaminant levels between diabetic and non-diabetic individuals, using age as a covariate. Variables that did not fit a normal distribution, as identified by the Shapiro-Wilk test, were normalized using the logit function.

A principal component analysis (PCA) based on a correlation matrix was used to cluster the contaminants together in order to reduce the large number of variables into component scores. The contaminants included in the PCA were those with a detection frequency of more than 60% and included HCB, Mirex, oxychlordane, DDE, HCH, trans-nonachlor, cis-nonachlor, Aroclor1260, ΣPCBs, Hg, and PBDE-47 and the factor loadings were determined for each variable. The first component axis scores were used in statistical analyses because it accounted for most of the variance in contaminant burden (Fig. S1, Supplementary data).

General linear models were used to determine the association between HOMA-IR or HOMA-β and POPs (represented by the PC 1 axis scores). Age, BMI and smoking status were also included in the model. The onset of diabetes results in a lower fasting insulin level. Therefore, to keep a linear correlation between HOMA-IR and HOMA-β and insulin resistance, only non-diabetic individuals (n = 46) were included in this analysis.

3. Results

3.1. Participant characteristics

There was a 36% prevalence of type 2 diabetes for the study participants (Table 1). The mean (±SD) age of diabetic individuals (50 ± 14) was significantly higher than non-diabetic individuals (39 ± 11). Of the non-diabetic participants, 54% were female and 62% of the diabetic participants were female. The mean (±SD) BMI of non-diabetic individuals (32 ± 4.9 kg/m²) was the same as the BMI of diabetic individuals (32 ± 4.8 kg/m²), and waist circumference also did not differ significantly between the two groups. Diet was quantified using a wild food index based on the frequency of wild food consumed and was not found to differ significantly with diabetic status. The mean HOMA-IR was found to be significantly higher for diabetic individuals (P < 0.05). The mean HOMA-β was found to be significantly higher for non-diabetic individuals (P < 0.05).

The mean (±SD) fasting glucose concentration was significantly higher for diabetic (9.0 ± 3.2 mmol/L) than non-diabetic (5.6 ± 0.6 mmol/L) individuals. The mean glucose response following the Oral Glucose Tolerance Test increased in both groups but was greater in diabetic than non-diabetic individuals (group × time interaction, P < 0.05; burden [Fig. S2, Supplementary data]). The mean (±SD) fasting plasma insulin levels did not differ between diabetic (91.6 ± 69.6 pmol/L) and non-diabetic (85.8 ± 50.0 pmol/L) participants. During the Oral Glucose Tolerance Test, insulin levels increased to a greater extent in the non-diabetic individuals (group × time interaction, P < 0.05).

### Table 1

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Non-diabetic (n = 46)</th>
<th>Diabetic (n = 26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>39 (36–42)</td>
<td>50 (45–55)</td>
</tr>
<tr>
<td>Sex (M:F)</td>
<td>21:25</td>
<td>10:16</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>91 (86–96)</td>
<td>87 (81–93)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>32 (31–34)</td>
<td>32 (30–34)</td>
</tr>
<tr>
<td>Waist Circumference (cm)</td>
<td>114 (110–118)</td>
<td>112 (107–118)</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>85</td>
<td>73</td>
</tr>
<tr>
<td>Diet (Wild food index)</td>
<td>47 (38–55)</td>
<td>59 (47–70)</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>0.055 (0.054–0.056)</td>
<td>0.074 (0.067–0.081)</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>3.1 (2.6–3.6)</td>
<td>5.4 (3.5–7.2)</td>
</tr>
<tr>
<td>HOMA-β</td>
<td>182.3 (92.7–271.8)</td>
<td>71.4 (51.6–91.2)</td>
</tr>
<tr>
<td>Plasma lipids (g/L)</td>
<td>6.8 (6.3–7.2)</td>
<td>6.7 (6.1–7.2)</td>
</tr>
</tbody>
</table>


* a No overlap of 95% CIs.
the same whether or not POPs with non-detects were replaced with random numbers during analyses.

Strong correlations were shown between all pollutants and age (0.15 ≤ R² ≤ 0.65; P < 0.05; data not shown) with the exception of PBDE-47. We therefore adjusted for the effect of age on all pollutants but PBDE-47 through an ANCOVA, where age was the covariate. Plasma levels of trans-nonachlor, oxychlordane, and DDE were significantly higher (P < 0.05) in diabetic individuals after age-adjustment. Age-adjusted cis-nonachlor and mercury levels were higher in diabetic than non-diabetic individuals, but fell short of statistical significance (β = −0.16, P = 0.06; β = −0.21, P = 0.07 respectively). The axis scores from the PC 1, after age-adjustment, were higher in diabetic participants but also fell short of statistical significance (β = −0.14, P = 0.08).

3.3. Inflammatory markers and diabetic status

None of the inflammatory markers differed between diabetic and non-diabetic groups (Fig. 1). The mean (±SD) TNF-α concentrations for diabetic and non-diabetic participants were 2.8 ± 3.9 pg/mL and 2.1 ± 1.4 pg/mL, respectively. In diabetic participants, the mean (±SD) IL-6 concentration was 3.3 ± 1.9 pg/mL and 4.2 ± 7.2 pg/mL in non-diabetic participants. The mean (±SD) total adiponectin concentration was 7.8 ± 5.3 μg/mL for diabetic individuals and 5.8 ± 2.4 μg/mL for non-diabetic individuals. For diabetic and non-diabetic individuals respectively, the mean (±SD) HMW adiponectin concentrations were 3.3 ± 2.9 μg/mL and 2.4 ± 1.3 μg/mL. The ratio of HMW to total adiponectin concentration was a mean (±SD) of 0.39 ± 0.09 for diabetic individuals and 0.39 ± 0.13 for non-diabetic individuals.

3.4. The association of POPs to insulin resistance/secretion

To associate insulin resistance to POPs and Hg, the PCA for contaminants was used. The PCA showed that 80% (PC 1 = 69%, PC 2 = 11%) of the total variance in contaminant levels was accounted for by the first two principle components. The PC 1 corresponded to a generalized contaminant burden since all factors loaded highly and positively. The PC 2 contrasted HCH and PBDE-47 (positive loadings) in one direction, and the remaining contaminants in another (Fig. S1, Supplementary data). For the non-diabetic group, we regressed a marker of insulin resistance, HOMA-IR, on age, BMI, smoking status and the first extracted pooled contaminant sample (PC 1). The full model accounted for 28% of the total variance in HOMA-IR (F[4, 41] = 3.95, P < 0.01) with only BMI making a statistical contribution to the model fit (β = 0.49, t = 3.66, df = 45, P < 0.001). We also regressed the marker of insulin secretion as quantified by HOMA-B on the same explanatory variables. The full model accounted only for 16% of the total variance in HOMA-β (F[4, 41] = 1.95, P = 0.12) with only BMI making a statistical contribution to the model fit (β = 0.30, t = 2.06, df = 45, P < 0.05). When the Matsuda, QUICKI or insulinogenic indices were used to quantify insulin resistance/secretion, similar results were obtained.
4. Discussion

4.1. Comparison of contaminants between diabetic and non-diabetic individuals

Mean average plasma levels of some POPs such as Mirex, Aroclor 1260, PCB 153, PCB 170, PCB 180 and PCB 187 are 2 to 7 times greater in our First Nations sample as compared to Caucasians of the same age and adiposity levels previously studied [32]. Concentrations of the POPs in our sample are comparable to published results based on a study of the Mohawk population of Akwesasne (in the St. Lawrence River area). Codru et al. [7] reported a mean (±SD) lipid-standardized concentration of PCB-153 of 104.5 ± 91.2 ng/g, compared to 178.8 ± 226.9 ng/g in our sample population. The mean (±SD) DDE concentration in our sample population (342.5 ± 410.4 ng/g) is lower than Akwesasne (537.0 ± 512.6 ng/g) but the mean (±SD) Mirex concentration in our sample (41.2 ± 64.5 ng/g) is higher than Akwesasne (19.2 ± 23.0 ng/g). In our sample population, age and lipid-adjusted plasma concentrations of some OC pesticides (i.e. oxychlordane, DDE, and trans-nonachlor) were higher in diabetic than non-diabetic individuals. These results corroborate epidemiological studies that have found higher concentrations of several pesticides in diabetic individuals. Diabetics had higher concentrations of oxychlordane, DDE, and trans-nonachlor in civilian, non-institutionalized participants from the USA [6], a remarkable similarity with the results described here. Also, the Mohawk population of Akwesasne had a significantly higher rate of diabetes at the highest tertile of exposure to DDE and HCB [7].

We did not see a difference in PBDE-47 levels between diabetic and non-diabetic individuals. This is corroborated by Turyk et al. [33] who found ΣPBDEs, PBDE-47, and PBDE-153 were not significantly higher in diabetic individuals. The tendency for Hg concentrations to be higher in diabetic individuals corroborates previous studies [11], Grandjean et al. [8] found no correlation between Hg and diabetes for Faroese marine food consumers, although the Hg levels here were derived from blood samples. The relationship between Hg and diabetes warrants further investigation.

4.2. Inflammatory marker levels

Several studies support the notion that inflammatory pathways are activated by pollutants [21]. Despite the fact that some OC pesticides (i.e. oxychlordane, DDE, and trans-nonachlor) were higher in our diabetic participants compared to non-diabetic participants, our results show no significant difference in levels of inflammatory markers between groups. Plasma adiponectin is generally lower in individuals with type 2 diabetes [34]. TNF-α and IL-6 are generally higher in diabetic individuals [35]. Of the 72 participants, 19 were on medication for hypertension and cardiovascular disease (CVD), which may have influenced the results as there could be a link between hypertension, IL-6, and TNF-α [36]. Also, some medications for hypertension and CVD could have modulated plasma levels of TNF-α, IL-6 [37], and adiponectin [38], even if not
taken the same day as the clinical session. This could obscure the expected correlation between harmful inflammatory markers and insulin resistance in non-diabetic subjects. As seen in Table 1, there was no difference in obesity between diabetic and non-diabetic individuals (and a lack of range in obesity), as measured through BMI. The correlation between adipokines and abdominal obesity may have further ensured a lack of correlation between POPs and inflammatory markers in this population.

4.3. POPs and insulin resistance/resistance

Because insulin resistance contributes to the development of type 2 diabetes, we examined whether POP levels were associated with surrogates for insulin resistance derived from fasting conditions (i.e. HOMA) and dynamic tests such as the Oral Glucose Tolerance Test in the non-diabetic group. Independent of the explanatory variables used, BMI was the only variable significantly accounting for 20% of the variance of insulin resistance. The correlation between BMI and insulin resistance is highly corroborated in the literature [39]. The high prevalence of obesity already reported in this sample [3] is thus most likely responsible for the high rates of type 2 diabetes.

Although our study found a lack of association between POPs and insulin resistance, other studies have reported such an association through animal models [40] and also in humans, as certain pesticides and PCBs were associated with insulin resistance in non-diabetic individuals [12]. If high plasma POP concentrations are not associated with insulin resistance, there should be an alternate explanation for why higher POP concentrations are seen in the diabetic group in our sample. Diabetic individuals metabolize lipids faster (through lipolysis) than non-diabetic individuals [41]. Usage of stored lipids has been shown to magnify contaminant concentrations in other tissues by releasing contaminants from lipid storage and into the bloodstream [42]. This may explain the higher plasma levels of pollutants seen in our diabetic participants.

For the non-diabetic group, the homeostasis model assessment of β-cell function, an index of insulin secretion, was regressed on the linear combination of age, BMI, smoking status and the first POP principal component. Our results revealed a non-significant contribution of POPs to the whole model. These results do not corroborate those of Jorgensen et al. [43] who noted that in the Inuit population of Greenland, POPs may affect β-cell function rather than stimulate insulin resistance. The potential effect of POPs on insulin secretion warrants further investigation.

Because of the cross-sectional nature of the study, we could not determine a causal relationship between pollutants and diabetes. However, a major strength of this study relies on the use of the Oral Glucose Tolerance Tests rather than self-reporting or simply fasting blood glucose values to identify people with diabetes. To our knowledge, this is also the first study that measured plasma inflammatory markers in conjunction with insulin resistance to explore the possible link to POP levels. These results represent an area of northwestern Ontario of limited study regarding diabetes and obesity.

5. Conclusions

This study shows that concentrations of certain pollutants in plasma are higher in diabetic than non-diabetic individuals in Northern Ontario First Nations communities. Despite some differences in plasma pollutant levels, no association was found between POP levels and surrogate indices for insulin resistance or insulin secretion. Adiposity level, quantified by BMI, is the major determinant of insulin resistance. Given this link, culturally-appropriate methods to reduce the prevalence of obesity in these communities should be introduced. Although the exact mechanisms remain unclear, this study confirms that the possible relationship between diabetes and pollutants warrants further exploration.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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Appendix A. Supplementary data

Supplementary materials (Fig. S1 and S2) associated with this article can be found at http://www.sciencedirect.com at http://dx.doi.org/10.1016/j.diabet.2013.01.006.

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