Characteristics of anemia and iron status and their associations with blood manganese and lead among children aged 3 to 19 years old from four First Nation communities in Québec

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Introduction

- Canada is among countries with the lowest prevalence of anemia (3%).
- This prevalence is invariably higher among its First Nations, particularly children[1].
- Childhood anemia is associated with growth, developmental, cognitive, psychomotor and immune system impairments.
- In First Nations communities, iron and other micronutrients deficiencies, infections and lead exposure are frequent, and possibly **risk factors** for **iron deficiency (ID) and anemia**[2].
- Higher intake of animal proteins (rich in bioavailable heme-iron), vitamin C (non-heme iron absorption enhancer), fruits and vegetables (rich in vitamins) are considered **protective factors** against ID and anemia[2].
- **Divalent metals** – manganese (Mn), zinc (Zn), cobalt (Co), cadmium (Cd) and lead (Pb) – **interact with iron** at different levels in human body[3].
- ID may upregulates the absorption and concentration of these metals inside human body, possibly increasing their toxicities[3].

Study objectives

1) Investigate the prevalence, types, and severity of childhood anemia and iron status by study nation, age, and gender
2) Examine protective and risk factors associated with anemia and ID
3) Study and document the possible associations between blood Mn, Zn, Co, Cd, Pb and iron biomarkers, considering relevant co-variables

Study design

- The study Youth Environment Study (YEH) was conducted among four First Nation communities in Quebec in Québec, Canada (see Figure 1)
  - Two Anishinabe communities (Abitibi-Temiscamingue region)
  - Two Innu communities (North Shore region)
- Transversal study conducted in May-June and Sept-Oct 2015, with 198 participants aged 3 to 19 years
- Data collected relevant for the present project:
  - Anthropometric measurements
  - Blood samples: Hemoglobin (Hb) (*in situ*), inflammatory biomarker (hs-CRP), and iron, Mn, Cd, Pb, Zn, Co biomarkers
- Individual questionnaires:
  - Socio-demographic
  - Food security & lifestyle
  - Food Frequency Questionnaires (FFQ) (traditional food & market foods)
  - Intakes calculated based on FFQ and food composition data

Table1: Divalent metals profile

	Manganese (Mn)	Zinc (Zn)	Cobalt (Co)	Cadmium (Cd)	Lead (Pb)
Role	Essential trace element and cofactor for many enzymes	Essential trace element, cofactor for many enzymes	Essential trace element entre in vitamin B12 synthesis	Xenobiotic	Xenobiotic
Source of exposure	Food, airborne, water, mining activities	Food, mining activities, steel smelting	Food, airborne due to metal smelting	Smoking, water ingestion, battery disposal	Old residential paints, hunting activities
Health effects	Neurobehavioral, memory and movement problem	Hematological, gastrointestinal effects, immunotoxic	Possibly carcinogenic to human	Chronic exposure carcinogenic	Attention, IQ, hematological & neurobehavioral

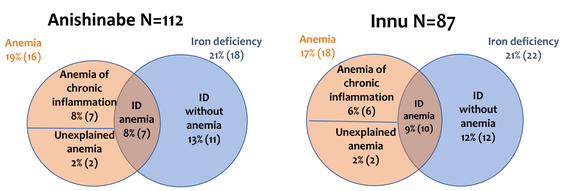
Figure 1: Studied First Nations and communities

Figure 2 :Statistical analysis

Objective (1) prevalence of anemia and ID	Descriptive statistics types of anemia and ID
Objective (2) risk factors for anemia and ID	Structural Equation Modeling
Objective (3) associations Mn, Zn, Co, Cd, Pb and iron	Multiple regression analysis for Iron biomarkers and Mn, Zn, Co, Cd and Pb

Results

Figure 3: Prevalence of anemia, anemia subtypes and ID by nation



Results are presented for193 participants, 5 participants were excluded due of missing data

Figure 4: Proportions of ID by age groups: YEH vs Canadian Health Measures Survey (CHMS)

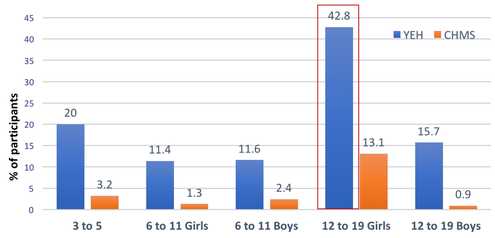
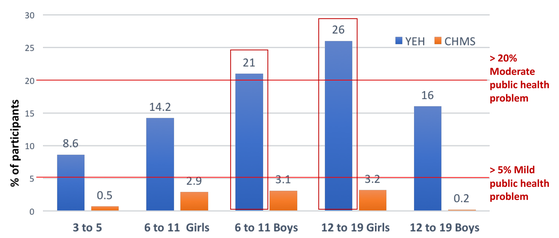


Figure 5: Proportions of anemia by age groups: YEH vs CHMS



Red lines refer to WHO reference values for public health significance of anemia [5,6]
Please note that CHMS coding for ID and anemia is slightly different than in the YEH project

Table 2: Results of the structural equation modeling/factorial analysis for protective and risk factors for Hb and ferritin

Factor	Standardized estimates for Hb (95%CI)	Standardized estimates for ferritin (95%CI)
Vegetables and fruits	0.13 (-0.38, 0.52)	0.13 (-0.16, 0.44)
Powder juice → vitamin C	**0.15 (0.004, 0.16)***	**0.15 (0.02, 0.27)***
Inflammatory markers	- 0.1 (-0.23, 0.04)	**0.12 (0.04, 0.18)***
Traditional meat	0.07 (-0.17, 0.32)	0.03 (-0.29, 0.36)
Market meat	0.02 (- 0.34, 0.37)	- 0.02 (-0.62, 0.59)

* : significant association for combined direct and indirect effects ($p < 0.05$)

- Higher intake of powder juice (fortified with vitamin C) and related vitamin C intake (an iron absorption enhancer) is associated with lower ID and anemia
- Models are controlled for household, age, sex , nation, interviewer and body mass index (BMI) and socioeconomic status

Table 3: Divalent metals in YEH by nation and compared to CHMS

Metal	Anishinabe (n=106) Geo mean (range)	Innu (n=84) Geo mean (range)
Blood Mn (µg/L)	15.33 (11.83, 18.83)	16.17 (12.71, 19.63)
Plasma Zn (µg/L)	1134.34 (980.38, 1288.30)	1081.87 (935.09, 1228.66)
Blood Co (µg/L)	0.26 (0.19, 0.33)*	0.18 (0.12, 0.25)
Blood Cd (µg/L)	0.51 (0.43, 0.58)	0.48 (0.40, 0.56)
Blood Pb (µg/L)	5.35 (3.51, 7.65)	7.21 (5.07, 9.87)*

* : significant difference between nation (T-test, $p < 0.05$)

- Exclusion of 3 participants based on liver diseases or dysfunctions
- Blood Mn is higher and blood Pb is lower than in CHMS (Cycle 2 or 3) (3-19 yrs old)

Figure 6: Significant associations between blood Mn, Co and serum ferritin concentrations (iron stores)

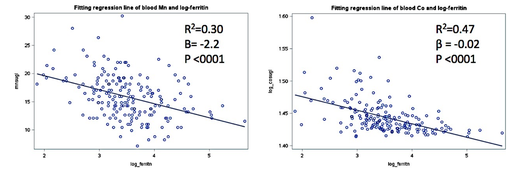
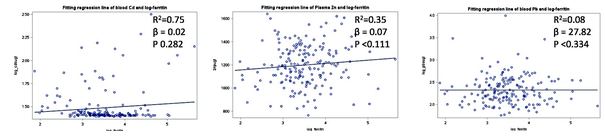


Figure 7: Insignificant associations between blood Cd, Zn, Pb and serum ferritin concentrations (iron stores)



Models are adjusted for age, sex, nation, education, household, interviewer, inflammatory biomarker, manganese ,iron , zinc and vitamin c intake, BMI, and sources of drinking water.

Conclusions

- ID and anemia are considerably higher than CHMS and comparable in both studied nations
  - ID is particularly high among 12-19 years old girls
  - According to OMS : anemia is a moderate public health problem among 6-11 years old boys and 12-19 years old girls
- Higher intake of powder juice (fortified with vitamin C) and related vitamin C intake (an iron absorption enhancer) is associated with lower ID and anemia
- High blood Mn concentrations is similar between nations and no environmental sources were identified
- Low blood Pb concentrations
- Blood Mn and Co concentrations correlates negatively with iron stores
- These preliminary findings suggest that increasing intake of vitamin C (from other sources than power juice which are excessively elevated in added sugar) would prevent ID, anemia and blood manganese

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