

ABSTRACT

Despite a high prevalence of anemia among non-pregnant Cambodian women, recent reports suggest iron deficiency prevalence is low. If true, iron supplementation will not reduce anemia.

In Phase I, we investigated factors associated with hemoglobin, ferritin, and soluble transferrin receptor (sTfR) concentrations in 450 women 18-45 years in Prey Veng province. Overall, 54% had a genetic hemoglobin disorder, 29.5% had anemia (hemoglobin <120 g/L), and 2% and 19% had iron deficiency based on ferritin (<15 µg/L) and sTfR (>8.3 mg/L), respectively. The hemoglobin E homozygous genotype was associated with 50% (95% CI: 14%, 96%) and 51% (95% CI: 37%, 66%) higher mean ferritin and sTfR concentrations as compared to normal hemoglobin structure. These findings challenged the diagnostic accuracy of ferritin and sTfR to estimate iron deficiency.

In Phase II, we measured the effect of oral iron (Fe) with or without multiple micronutrients (MMN) on hemoglobin concentration as a direct way to determine the extent to which iron deficiency (or other micronutrient deficiencies) was a cause of anemia. A total of 809 non-pregnant women 18-45 years with hemoglobin ≤117 g/L (HemoCue®) were recruited from Kampong Chhnang province to a 2x2 factorial double-blind randomized trial. Women received 12 weeks of daily Fe (60 mg), MMN (14 other micronutrients), Fe+MMN, or placebo capsules. Baseline anemia prevalence was 58% (Sysmex analyzer). Mean (95% CI) hemoglobin at 12 weeks did not differ in the Fe and Fe+MMN groups (121 [120, 122] vs. 123 [122, 124] g/L); both were higher than MMN and placebo (both 116 [115, 117] g/L, $P<0.05$). Mean (95% CI) increase in hemoglobin was 5.6 (3.8, 7.4) g/L ($P<0.001$) among women who received Fe ($n=383$) and 1.1 (-0.7, 2.9) g/L ($P=0.24$) among women who received MMN ($n=382$), with no interaction between interventions ($P=0.61$). At 12 weeks, 19% and 30% of women had a hemoglobin response ≥10 g/L in Fe and Fe+MMN groups, compared to 8% and 5% in MMN and placebo, respectively.

Daily iron supplementation for 12 weeks increased hemoglobin in non-pregnant Cambodian women; however, MMN did not confer additional benefit. Only ~25% of our predominantly anemic study population was responsive to iron.

BIOGRAPHICAL NOTES

Academic Studies: MSc, University of Toronto, 2010
BSc, University of British Columbia, 2001

GRADUATE STUDIES

Field of Study: International Nutrition

Courses

HUNU 500 Research Methods
HUNU 631 Food, Nutrition, and Health Seminar

Instructors

Dr. Chapman
Various

SELECTED AWARDS

- Vanier Scholarship, Canadian Institutes of Health Research, 2014
- Career Enhancement Award, Canadian Child Health Clinician Scientist Training Program, 2014
- Michael Smith Foreign Study Supplement, Canadian Institutes of Health Research, 2014
- Emerging Leaders in Nutrition Science Poster Competition Award, Global Nutrition Council of the American Society of Nutrition, 2015
- Outstanding Achievements for a Doctoral Candidate Award, BC Children's Hospital Research Institute, 2016
- Early Career Contribution to Alleviation of Micronutrient Malnutrition, International Life Sciences Institute, 2016

SELECTED PUBLICATIONS

Karakochuk CD *et al.* Comparison of four immunoassays to measure serum ferritin concentrations and iron deficiency prevalence among non-pregnant Cambodian women and Congolese children. *Clin Chem Lab Med* 2017 (in press).

Karakochuk CD *et al.* The homozygous hemoglobin EE genotype and chronic inflammation are associated with high serum ferritin and soluble transferrin receptor concentrations among women in Cambodia. *J Nutr* 2015; 145: 2765-73.

Karakochuk CD *et al.* Elevated levels of iron in groundwater in Prey Veng province in Cambodia: a possible factor contributing to high iron stores in women. *J Water Health* 2015; 13(2): 575-86.

Karakochuk CD *et al.* Evaluation of two methods to measure hemoglobin concentration among women with genetic hemoglobin disorders in Cambodia: a method-comparison study. *Clin Chim Acta* 2015; 441: 148-55.

Karakochuk CD *et al.* Genetic hemoglobin disorders rather than iron deficiency are a major predictor of hemoglobin concentration in women of reproductive age in rural Prey Veng, Cambodia. *J Nutr* 2015; 145: 134-42.



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THE UNIVERSITY OF BRITISH COLUMBIA

Graduate and Postdoctoral Studies

SELECTED PRESENTATIONS

Inherited hemoglobin disorders are associated with high serum hepcidin concentrations in Cambodian women of reproductive age [Poster]. American Society of Human Genetics Annual Meeting 2016, Vancouver, Canada.

The effect of oral iron with or without multiple micronutrients on hemoglobin concentration among non-pregnant Cambodian women of reproductive age: A 2x2 factorial double-blind randomized controlled supplementation trial [Poster]. Micronutrient Forum 2016, Cancun, Mexico.

α -1 acid glycoprotein but not C-reactive protein is associated with lower serum zinc concentrations among Congolese children aged 6-59 months and has a substantial impact on prevalence of zinc deficiency [Poster]. *FASEB Journal* 2016; 30(1): 688.1. Experimental Biology 2016, San Diego, USA.

An evaluation of two methods to measure hemoglobin concentration among women with genetic hemoglobin disorders in Cambodia: A method comparison study [Poster and Oral]. *FASEB Journal* 2015; 29(1): 403.1. Experimental Biology 2015, Boston, USA.

A lack of iron deficiency despite a high prevalence of anemia among women in rural Cambodia and the associated factors of genetic hemoglobin disorders and inflammation [Poster]. *Applied Physiology, Nutrition, and Metabolism* 2015; 40(5): 514-5. Canadian Nutrition Society Annual Conference 2015, Winnipeg, Canada.

Genetic hemoglobin disorders and anemia in Cambodian women [Poster]. *European Journal of Nutrition & Food Safety* 2015; 5(5): 402-3. Micronutrient Forum 2014, Addis Ababa, Ethiopia.

Genetic hemoglobin disorders and anemia in Cambodian women of reproductive age [Oral]. *FASEB Journal* 2014; 28(1): 389.7 Experimental Biology 2014, San Diego, USA.

PROGRAMME

The Final Oral Examination
For the Degree of

DOCTOR OF PHILOSOPHY
(Human Nutrition)

CRYSTAL D KARAKOCHUK

MSc Nutritional Sciences, University of Toronto, 2010
BSc Dietetics, University of British Columbia, 2001

Wednesday, December 7, 2016, 12:30 pm
Room 200, Graduate Student Centre
Latecomers will not be admitted

“Is Iron Deficiency a Major Cause of the High Prevalence of Anemia in Non-pregnant Cambodian Women of Reproductive Age? Evidence from a Cross-sectional Survey and a Randomized Controlled Trial”

EXAMINING COMMITTEE

Chair:

Dr. Emma Guns (Experimental Medicine)

Supervisory Committee:

Dr. Timothy J Green, Research Supervisor (Human Nutrition) Dr.

Susan I Barr (Human Nutrition)

Dr. Suzanne M Vercauteren (Pathology and Laboratory Medicine)

University Examiners:

Dr. Zhaoming Xu (Human Nutrition)

Dr. Joel Singer (Population and Public Health)

External Examiner:

Dr. Janet C King

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