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Validity of the Willett food frequency questionnaire in assessing the iron intake of French-Canadian pregnant women

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ABSTRACT

Objective: Maternal intake is crucial to pregnancy outcomes. Evidence shows that both nutrient deficiency and excess can have adverse effects. In pregnancy, changes in iron metabolism occur; therefore, dietary reference intakes increase to support expansion of red cells and maternal–fetal transfer of iron. Appropriate and valid assessment tools are required to investigate nutritional concerns in mothers with and without gestational diabetes mellitus (GDM). The objective of this study was to assess the Willett food frequency questionnaire (FFQ) to assess iron intake in women with (n = 15) and without (n = 45) GDM.

Methods: To validate the modified FFQ, estimated total iron intake during the third trimester was compared with biomarkers of iron status such as serum ferritin, soluble transferrin receptor (sTfR), and the sTfR:F index at delivery. Data were tested for normality using the D'Agostino-Pearson test. Differences between groups were tested using *t* tests or Mann–Whitney tests. Correlations were tested using Spearman's ρ. Significance was set at $P < 0.05$.

Results: Significant crude and energy-adjusted serum ferritin and total iron intake were related ($\rho = 0.30$; $P < 0.05$) in women without GDM. Serum ferritin, sTfR, and the sTfR:F index were different ($P < 0.05$) between women with intakes above and below the recommended levels. Cross-classification showed agreement between methods in mothers with and without GDM; on average, 63% of the women were classified into the same or adjacent quartile when ranked by FFQ and iron status.

Conclusion: These findings suggest the Willett FFQ is a good tool for assessing total iron intake of French-Canadian pregnant women.

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Introduction

Iron plays a key role in hemoglobin and myoglobin synthesis, as well as in the function of a wide range of iron-dependent enzymes, making it essential throughout the life cycle [1]. In pregnancy, important changes in iron metabolism occur, including the expansion of maternal red cell mass and the deposition of substantial amounts of iron in the fetus and placenta. Maternal iron status is dependent on several factors that likely attenuate associations between iron intake and biochemical markers of iron status [2] such as measurement errors and a lack of knowledge regarding time–effect and dose–response relationships. Requirements for absorbed iron increases from 0.8 mg/d in the first trimester to 7.5 mg/d in the last trimester of pregnancy, resulting in a total iron requirement of approximately 1240 mg in normal pregnancy [3]. Notable changes are observed in iron absorption and serum ferritin, the principal storage form of iron [3,4]. Iron absorption is influenced by factors other than simply the amount consumed from foods and supplements, such as iron bioavailability, the trimester of pregnancy, and maternal body iron stores. In response to the increased need for iron, intestinal iron absorption also increases throughout pregnancy, which is inversely correlated with serum ferritin [3,5].

MC, J-CF, and YG, are responsible for the Healthy Pregnancy infrastructure; they also participated in the preparation of the manuscript. The study was designed and funding secured by HW. HV managed the study from ethics to selection of the study participants and measurement of biochemical markers of iron status. The design and conduct of the statistical analyses and preparation of this manuscript was accomplished by SB and CV under the supervision of HW.

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Serum ferritin gradually declines to reach its lowest concentration (~12 μg/L) at 35 wk to 38 wk of pregnancy, followed by a moderate increase toward delivery; however, these changes are physiological and do not necessarily reflect iron balance [3]. Ferritin also is increased in proportion to supplementation and infection, whereas soluble transferrin receptor (sTfR), a sensitive marker of iron deficiency, and the ratio of sTfR to ferritin (sTfR:F) only rises when the supply of iron to the erythrocytes fails due to exhausted iron stores [3]. Including measurement of sTfR:F are useful in identifying women with low serum ferritin with pronounced iron deficiency [3,4]. Iron intake is the only modifiable factor affecting iron status during pregnancy; therefore, it is important to evaluate the ability of dietary assessment tools to assess accurately iron intake in pregnant women.

Assessment of maternal nutrient intake is crucial due to the increasing evidence that both nutrient deficiency and excess can have adverse effects on pregnancy outcomes [6]. Poor fetal nutrition may contribute to the development of hypertension and other chronic diseases through fetal programming [7], and conditions such as gestational diabetes mellitus (GDM) can compromise the iron status of newborn infants, consequently impairing cognitive development [8–10]. GDM is one of the most common complications of pregnancy and affects approximately 4% of all pregnancies in the general Canadian population [11]. Appropriate and valid dietary assessment tools are required to investigate possible nutritional concerns in mothers with and without GDM.

Food frequency questionnaires (FFQs) are designed to provide an estimate of the habitual diet [12] and have been widely used for assessing diet in a variety of contexts [12–14], including pregnancy [15–17] and validated against other dietary assessment methods [2,12,18]. However, biomarkers are an objective means of assessing nutrient status, and the measurement errors are not correlated with measurement errors in self-reported dietary assessment methods. For nutrients with biochemical markers that are responsive to intake, a correlation between a reported dietary intake and an objective biochemical measure can be interpreted as the lower bound of the true questionnaire validity [2,19]. For most nutrients, correlation coefficients with biomarkers are in the range of $r = 0.3$ to 0.5 [20].

This study examines the relationship between biomarkers of iron status and dietary intake of iron including supplemental iron intake, in order to determine the relative validity of the Willett FFQ in assessing maternal iron intake during gestation.

Materials and methods

Study design and subjects

This study is part of a case–control study on the effects of GDM on the iron and long-chain polyunsaturated fatty acid (LC-PUFAs) status of newborn infants from mothers with GDM, to be reported separately. Participants were selected from a large, ongoing prospective cohort study of pregnant women and their newborns conducted in Québec City, Québec, Canada. Briefly, this cohort is comprised of women who visited the perinatal clinics at Centre Hospitalier Universitaire de Québec. Between September 2007 and April 2009, women with and without GDM were identified from a cohort study and asked to participate in this case–control study (1:3 allocation) that required completion of the FFQ. Inclusion criteria comprised women in general good health, without chronic disease, having delivered one baby, and manifesting the intent to breastfeed the infant. Women with continuous smoking and/or alcohol consumption during pregnancy, with asthma or infection at delivery, who suffered from hypertensive disorders of pregnancy, who were showing complications of diabetes mellitus, or those who deliver a small-for-gestational age baby were excluded from the study. Following delivery, women were asked to participate in this substudy by a research nurse. Blood samples; sociodemographic and biomedical information; and data on weight gain, nutrition, and dietary supplement use were collected. GDM is a common but serious complication of pregnancy; therefore, we chose to include mothers with GDM in the present study [21].

Dietary assessment

Dietary intake was assessed by the semi-quantitative FFQ developed by Willett et al., which has previously been validated for pregnant women in the United States [16]. In order to make the tool appropriate for Canadian pregnant women in Québec, and because the Willett FFQ was initially designed for Americans, a translation was conducted from English to French, taking care to respect language particularities occurring in Québec, by three bilingual experts in the field of nutrition and dietetics. Mothers were given the FFQ postnatally, before discharge and were asked to report the frequency of consumption of the food items listed on the FFQ during their third trimester of pregnancy. A trained nurse provided mothers with instructions related to portion sizes and frequencies of consumption. The questionnaire contains 116 food items and 11 additional questions regarding the frequency of use of multivitamin/mineral and other supplements. For the food items, the frequency intervals ranged from never, up to six times per d (never, less than once per mo, one to three times per mo, one to two times per wk, three to four times per wk, five to six times per wk, daily, two to three times per d, four to five times per d, and six or more per d). All reported frequencies were then converted to frequencies per d.

Calculation of nutrient intakes

Nutrients derived from the FFQ were estimated using the Canadian Nutrient File (version 2007b) to calculate the daily intake of nutrients from foods, as this database reflects Canadian food composition data. Manufacturer specifications were used to estimate the nutrient content of supplements. The total daily intake of iron (g/d) was calculated, and energy-adjusted dietary iron intake was calculated using the nutrient density method proposed by Willett [22]. Intake of iron from supplements is not related to energy intake (EI), as would be the case with iron derived from food, therefore, we did not adjust the EI of iron from supplements or for total iron intake. The energy-adjusted dietary iron intake was added to the raw value of iron intake from supplements in order to get a single value for total iron intake [23]. Finally, the total iron intake of subjects was compared to both the Recommended Dietary Allowances (RDA) and the Estimated Average Requirements (EAR) for iron during pregnancy in order to evaluate the prevalence of inadequate iron intake of the study group [24]. The proportion of women above and below the RDA and the EAR were calculated because these recommendations are set based on dietary intake data and are meant to represent healthy levels of intake [25].

Iron assessment

Venous blood samples were collected into lithium heparin tubes by hospital staff from each mother at hospital admission for delivery. Blood was immediately processed and plasma was extracted and frozen at −80°C until analysis. Ferritin was measured in 10 μl of plasma using an autoanalyzer (Liaison, DiaSorin, Vercelli, Italy). Replicate analysis of standards yielded a coefficient of variation of $< 5\%$ for this assay. sTfR was measured in 20 μl of plasma in duplicate using the quantikine IVD soluble transferrin receptor enzyme-linked immunosorbent assay (R&D systems, Minneapolis, USA). A coefficient of variation $<15\%$ was acceptable according to manufacturer instructions. The sTfR:F index was calculated as the ratio of sTfR concentration to the logarithm of ferritin concentration sTfR (mg/L):log ferritin (μg/L) as it is suggested to be the best estimate of body iron, regardless of the presence or absence of inflammation in the patient [24].

Ethical approval

All participants gave informed consent and all procedures were approved by the McGill Institutional Review Board of the Faculty of Medicine as well as by the Centre Hospitalier Universitaire de Québec Ethics Review Board.

Statistical analysis

Data were analyzed for the total sample and in subgroups of healthy women and women with GDM to rule out possible alterations in iron metabolism in GDM associated with higher maternal–fetal transfer of iron. When data subsets were not normally distributed according to the D'Agostino-Pearson test for normality, both parametric and non-parametric tests were used. Differences between non-GDM and GDM groups were tested using *t* tests or Mann Whitney U tests. The crude and energy-adjusted Spearman rank correlation coefficients between daily iron intake and biomarkers of iron status were calculated to determine the degree of agreement between total iron intake and iron status. As proposed by Block [26], the percentage of agreement between both variables was further examined by classification of absolute iron intakes divided into quartiles. We constructed quartiles according to the distribution in the study population of total iron intake and cross-tabulated this data with its respective biomarkers to

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