The Role of Diet in Predicting Iron Deficiency Anemia in HIV-Positive Women

LADAN SHAHVARANI RENOUF, RD, MSc, SAMUEL SHEPS, PhD, School of Population and Public Health, University of British Columbia, Vancouver, BC; **ANITA HUBLEY, PhD,** Department of Education and Counselling Psychology, and Special Education, University of British Columbia, Vancouver, BC; **NEORA PICK, MD,** Division of Infectious Diseases, University of British Columbia, Vancouver, BC; **DIANA JOHANSEN, RD,** Children's & Women's Health Centre of British Columbia, Vancouver, BC; **MARK W. TYNDALL, MD, ScD, FRCPC,** Division of Infectious Diseases, University of Ottawa, Ottawa, ON

ABSTRACT

Purpose: The association between medical, social, and nutritional factors and iron deficiency anemia was examined in adult women who had tested positive for human immunodeficiency virus (HIV) and were living in the Greater Vancouver Area.

Methods: This was a cross-sectional observational study of 102 HIV-positive women, aged 19 or older, who were patients of one of three chosen community health clinics in Vancouver, British Columbia. Information on usual dietary intake and other nutrition-related factors was collected with a short diet survey, while medical information and laboratory data were obtained from each participant's medical chart.

Results: Of the predictors studied, a CD4 cell count below 200 cells/µL, a regular menstrual pattern, and African ethnicity were associated with an increased risk of iron deficiency anemia. Dietary intake was not independently associated with iron status.

Conclusions: Iron deficiency anemia in HIV-positive women has multifactorial and complicated causation, but is strongly associated with poorer immune status and greater menstrual losses. Health disparities in Aboriginal and African women may lead to a higher risk for iron deficiency anemia. Routine screening and ongoing nutrition education are necessary for the prevention and management of iron deficiency anemia. Further research into factors associated with iron deficiency anemia is essential to improve prevention and management efforts.

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RÉSUMÉ

Objectif. L'association entre les facteurs médicaux, sociaux et nutritionnels et l'anémie ferriprive a été étudiée chez des femmes adultes porteuses du virus de l'immunodéficience humaine (VIH) résidant dans la région du Grand Vancouver.

Méthodes. Une étude d'observation transversale a été effectuée auprès de 102 femmes porteuses du VIH âgées de 19 ans et plus et qui étaient des patientes de l'une des trois cliniques de santé communautaire sélectionnées à Vancouver, Colombie-Britannique. De l'information sur l'apport alimentaire habituel et d'autres facteurs en lien avec la nutrition a été recueillie à l'aide d'une courte enquête sur l'alimentation, et l'information médicale et les données de laboratoire ont été tirées du dossier médical de chaque participante.

Résultats. Parmi les prédicteurs étudiés, une numération des cellules CD4 inférieure à 200 cellules/µl, un cycle menstruel régulier et une origine ethnique africaine étaient associés à une augmentation du risque d'anémie ferriprive. Toutefois, il n'existait pas d'association indépendante entre l'apport alimentaire et le bilan en fer.

Conclusions. L'anémie ferriprive chez les femmes porteuses du VIH est caractérisée par des causes multifactorielles et complexes, mais est fortement associée à un faible état immunitaire et à des pertes menstruelles plus abondantes. Les disparités sur le plan de la santé chez les femmes autochtones et africaines pourraient générer un risque accru d'anémie ferriprive. Un dépistage régulier et de l'éducation à la nutrition continue sont requis pour la prévention et la gestion de l'anémie ferriprive. D'autres recherches sur les facteurs associés à l'anémie ferriprive sont essentielles afin d'améliorer les efforts de prévention et de gestion.

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INTRODUCTION

Anemia, defined as a hemoglobin concentration below 120 g/L in women and below 140 g/L in men, is the most common comorbidity associated with human immunodeficiency virus (HIV) infection (1,2). The prevalence of anemia increases proportionately as HIV disease progresses and CD4 cell count is reduced to 200 cells/µL or lower (3). Iron deficiency without anemia represents a moderate depletion of iron stores, marked by ferritin levels below 30 µmol/L, but without reduced hemoglobin concentration (4). If untreated, iron deficiency leads to iron deficiency anemia, characterized by reduced reticulocytes, hemoglobin, hematocrit, and storage iron markers such as ferritin and transferrin saturation (4), as well as small (microcytic) and pale (hypochromic) reticulocytes (5-7).

Anemia may reflect social inequity.

The major cause of anemia in those with HIV is blood loss often associated with inflammation, bone marrow suppression, and disruption of intestinal epithelial cell replication (8). Women who have tested positive for HIV also show a higher prevalence of anemia (55%) than do men who have tested positive (45%); this finding is related to greater iron losses during menstruation and pregnancy (1,8,9). Despite major developments in and wider access to highly active antiretroviral therapy, the prevalence of anemia remains relatively unaffected (8,10), which suggests anemia may reflect social inequity as well as an HIV comorbidity (11).

PURPOSE

Untreated anemia has deleterious effects on quality of life, HIV progression, and overall survival (2,3,8,10-12). Although several studies have shown the prevalence, incidence, and risk factors for anemia in HIV-positive women, no investigators have attempted to explore the role of nutrition in its etiology (2,9,12,13). We examined the association between particular medical, social, and nutritional factors and the likelihood of iron deficiency anemia in a sample of HIV-positive women, and sought to determine whether a direct relationship exists between iron intake and iron status.

METHODS

Participants

Of 104 participants recruited from three community health clinics and one acute care facility in Vancouver, two with incomplete laboratory measures were removed from data analysis. Thus, results are based on data from 102 participants. A representative sample of women was achieved by including participants from both inner-city clinics (where substance abuse and poverty are more prevalent) and hospital-based clinics (where participants were more likely to be employed and supported within a family unit). Overall, participants recruited were representative of sociodemographic characteristics of the clientele at each location.

Inclusion criteria were female sex, confirmed HIV-positive status, age at least 19 years, no current pregnancy, and a CD4 cell count of at least 200. Although iron deficiency anemia prevalence is greatest among women of childbearing age, menopausal and perimenopausal women were also included due to evidence of iron deficiency anemia risk with longer duration of HIV infection (2,9).

Study procedures

Cross-sectional, multicentre data were gathered from January 2009 to May 2009. Ethics approval was obtained from the ethics boards of the University of British Columbia, Providence Health Care, Vancouver Coastal Health, and Children's and Women's Hospital of British Columbia. Clinic staff members were informed of the study protocol and assisted in recruiting eligible participants. Informed written consent was obtained from all participants. An honorarium of $10 was provided to all participants who signed the consent form.

The same interviewer conducted all the surveys with participants, using a newly designed survey based on a list of commonly consumed iron-containing foods drawn from the National Health and Nutrition Examination Survey food frequency questionnaire (FFQ) and the Canadian Nutrient File (CNF) (14-16). This tool included an FFQ, as well as questions on supplement use, menstrual pattern, vegetarian status, food preparation methods, and food insecurity. The survey took 20 minutes to administer.

Chart records were reviewed for body mass index (BMI), other medical conditions, immune status, and anemia-related laboratory measures. All laboratory values taken within the preceding three months were included, as were new measures ordered by the physician, as needed.

If hemoglobin levels were within the normal range (>120 g/L), iron deficiency anemia was ruled out without further investigation. Iron deficiency anemia was diagnosed in the presence of low levels of hemoglobin (<120 g/L) and ferritin (<30 μmol/L) (5,7).

Diet survey design

The diet survey was a semiquantitative FFQ based on 65 commonly consumed foods containing iron. However, the survey was designed to track the number of times a food was consumed over the preceding seven days, rather than the traditional one-month interval. The rationale for this was to preserve memory recall as much as possible (14). Serving size for each item was derived from the CNF, as these serving sizes correspond to common measures of dietary intakes (16). To calculate total estimated daily iron intake, we multiplied the intake of each food item by its iron content, as estimated from the CNF (16). This value was then divided by seven to calculate average daily intake.

Data analysis

For all statistical analyses, the statistical software program S-PLUS 8 Enterprise Developer for Windows (Insightful Corporation, Seattle, WA, 2007) was used. For descriptive purposes, the sample was categorized into two groups, namely those with iron deficiency anemia and those without. Analysis of variance and *t*-tests were conducted for continuous variables and chi-square tests for categorical variables.

A multiple logistic regression model was used to adjust for factors associated with iron deficiency anemia, including iron intake (mg/day), CD4 below 200 cells/μL, ethnicity, intravenous (IV) drug use, and menstrual pattern. Nutritional factors included multivitamin and iron supplement use, vegetarianism, and use of food assistance programs. Regression coefficients were obtained for each of the independent variables, which were then converted to odds ratios (ORs), and significance was in-

Table 1
Characteristics of study participants with and without iron deficiency anemia (continuous variables)

	With anemia (n=16)		Without anemia (n=86)		
Characteristic	**Mean**	**SD**	**Mean**	**SD**	**p value**
Mean age (years)	40.3	9.1	41.3	7.4	0.62 (NS)
Body mass index (kg/m^2)	23.7	6.6	24.0	5.2	0.84 (NS)
Estimated iron intake (mg/day)	13.3	4.6	13.1	6.4	0.48 (NS)
Hemoglobin (g/L)	108.6	9.1	128.6	13.4	<0.001[a]
Mean corpuscular volume (fL)	86.2	8.0	93.0	9.0	0.03[a]
	Median	**Range**	**Median**	**Range**	
CD4 (cells/μL)	340	40-810	380	10-940	0.11 (NS)
Ferritin (μg/L)	11.0	3.0-40.0	58	10-344	<0.001[a]
Transferrin (g/L)	2.73	1.3-3.5	2.04	1.0-2.5	0.18 (NS)
Transferrin saturation (%)	9.0	5.0-22.0	17.0	4.0-30.0	0.04[a]

NS = nonsignificant; SD = standard deviation
[a] p<0.05

dicated by the 95% confidence interval. The multiple logistic regression model was also analyzed for significance using the likelihood ratio test and corresponding p value at α=0.05.

RESULTS

Data were collected for 102 participants, 60% of whom were recruited from Oak Tree Clinic, 25% from Vancouver Native Health Clinic, 11% from the Downtown Community Health Clinic Maximally Assisted Therapy program, and 4% from St. Paul's Hospital. Participants were predominantly Caucasian (53%), followed by Aboriginal (30%), African (11%), South Asian (4%), and Asian (2%) participants.

Hemoglobin levels were available for all participants, but ferritin levels were available for only 42, as criteria for testing iron storage parameters at clinics indicated these would be ordered only in the presence of anemia. Anemia prevalence was 30%, iron deficiency prevalence was 40%, and iron deficiency anemia prevalence was 16%. Twenty-two (52%) of those for whom ferritin levels were available had ferritin levels below 30 μg/L.

Tables 1 and 2 provide the overall distribution of characteristics for participants with and without iron deficiency anemia. Women with iron deficiency exhibited significantly lower levels of hemoglobin, mean corpuscular volume, ferritin, and transferrin saturation in comparison with women who did not have iron deficiency anemia (Table 1). Participants had a healthy BMI overall; only 22% had a BMI below 20 kg/m^2.

Women with iron deficiency anemia were predominantly of Aboriginal, African, or South Asian ethnicity, although the sample size was small in the latter two groups (Table 2). Most (75%) participants used antiretroviral therapy, and no current

Table 2
Characteristics of study participants with and without iron deficiency anemia (categorical variables)

Characteristic	With anemia (n=16)	Without anemia (n=86)	p value for difference
Ethnicity			
Caucasian (n=56)	5 (28%)	51 (60%)	Reference
Aboriginal (n=30)	5 (28%)	25 (29%)	0.31 (NS)
African (n=10)	4 (22%)	6 (7%)	0.02[a]
Asian (n=3)	1 (5%)	2 (2%)	0.28 (NS)
South Asian (n=3)	1 (17%)	2 (2%)	0.28 (NS)
Past/present intravenous drug use	2 (12%)	36 (42%)	0.03[a]
Hepatitis C virus	5 (31%)	42 (49%)	0.28 (NS)
Menstruation	13 (81%)	40 (46%)	0.08 (NS)
Regular	13 (81%)	32 (37%)	0.02[a]
Irregular	0 (0%)	7 (8%)	0.28 (NS)
Amenorrhea	5 (31%)	45 (52%)	0.03[a]
Number of days (range)	4.0 (0.0-7.0)	0.0 (0.0-8.0)	<0.001[a]
Past/present vegetarianism	5 (31%)	20 (23%)	0.53 (NS)
Iron supplement use	5 (31%)	20 (23%)	0.53 (NS)
Multivitamin supplement use	11 (69%)	47 (55%)	0.44 (NS)
Food assistance program use	10 (63%)	52 (60%)	0.90 (NS)

NS = nonsignificant
[a] p<0.05

opportunistic infections were indicated. Active IV drug use (37%) and hepatitis C positive status (46%) were prevalent in the sample as two health clinics were situated in Vancouver's Downtown Eastside. The prevalence of past or present vegetarianism was low (25%), although vegetarianism prevailed among South Asian women (100%). Multivitamin use was high (57%), but of 16 participants with iron deficiency anemia, only five were taking iron supplements (28%). Mean dietary iron intake from meat was 0.14 mg/day, with the majority of dietary iron derived from grain sources.

Food insecurity was a major issue for African women.

Table 2 also shows that 62 participants had used food assistance programs over a one-month period (61%), with most accessing food banks (68%). The use of food assistance programs was highest among Aboriginal women (90%), a difference that was significant when this group was compared with Caucasian participants (chi-square p value = 0.04).

Results of the logistic regression are provided in Table 3; each variable is adjusted in a multiple logistic regression model. Significant predictors for iron deficiency anemia included African ethnicity, regular menstrual pattern, and CD4 cell count below 200 cells/µL. No significant association was found between dietary iron intake and iron status.

DISCUSSION

The objectives of this study of HIV-positive women were to examine medical, social, and nutritional factors that have an impact on the likelihood of iron deficiency anemia, and to determine whether a relationship existed between dietary iron intake and iron status.

Predictors for iron deficiency anemia

Significant predictors for iron deficiency anemia included African ethnicity, a regular menstrual pattern, and a CD4 count below 200 cells/µL, a finding supported by previous studies (2,9). The finding that women of African ethnicity were nearly nine times as likely as Caucasian women to have iron deficiency anemia leads to the question of whether socioeconomic disparities may play a role, particularly because the African women in our sample were all new immigrants to Canada. Although thalassemia may often lead to anemia in the African population, this was not an issue in our sample. Because food insecurity was a major issue for African women in our study, it may have contributed to higher iron deficiency anemia rates in this group. However, the sample size was too small to draw definitive conclusions.

Women with CD4 counts below 200 cells/µL were almost nine times as likely to have iron deficiency anemia, and the link between CD4 count and anemia is well substantiated (2,9,12,17). Some potential mechanisms may be bone marrow suppression, chronic inflammation, malabsorption of nutrients, and a greater likelihood of opportunistic infections with advanced HIV stage (8,9).

Menstrual pattern has not been researched as widely in HIV-positive women, but may be a significant factor in iron status. In terms of menstrual cycle, little difference seems to exist between HIV-positive and HIV-negative women, although higher viral loads and lower CD4 cell counts may result in cycle variability and polymenorrhea (18). Thus, a biological interaction between low CD4 and increased menstruation may worsen iron status.

Table 3
Adjusted iron intakes and predictor variables

Variable	OR	95% CI	p value for OR
Estimated iron intake (mg/day)	1.03	(0.92, 1.17)	0.57 (NS)
Ethnicity			
Caucasian	1.00	Reference variable	
Aboriginal	1.12	(0.21, 6.1)	0.89
African	8.6	(1.1, 68.0)	0.04[a]
Asian	17.1	(0.63, 463)	0.09
South Asian	11.7	(0.32, 428)	0.18
Intravenous drug use	0.47	(0.06, 3.8)	0.48
Menstruation			
Regular	8.1	(1.5, 44.0)[a]	0.02[a]
Amenorrhea	1.00	Reference variable	
CD4 (<200 cells/µL)	8.8	(1.7, 46)[a]	0.01[a]
Multivitamin use	2.15	(0.47, 9.8)	0.32
Iron supplement use	3.1	(0.57, 17.0)	0.21
Vegetarianism	2.0	(0.44, 9.0)	0.37
Food assistance program use	3.0	(0.52, 17.0)	0.22

CI = confidence interval; NS = nonsignificant; OR = odds ratio
[a] $p<0.05$

Further research on and investigation of this relationship are needed.

Because the rate of IV drug use was nearly 40% in our sample, we explored the potential relationship between it and menstrual cycle disruption. Although substance use may result in shorter cycle length in women with HIV, amenorrhea is not commonly reported (17). In our sample, regular menstruation, rather than IV drug use, likely is a major predictor of iron status in HIV-positive women (19-23).

The rate of IV drug use was nearly 40%.

Potential confounders

When dietary iron intake was adjusted for other potential confounders, it showed no relationship to iron status (adjusted OR=1.03). No differences in this relationship were observed with adjustment for iron absorption factors (enhancers and inhibitors) because, for the majority of the sample, iron intakes were too low to enable the detection of differences (21). Furthermore, iron intakes from meat were much lower (0.14 mg/day) than in studies of HIV-negative women (0.8 to 1.0 mg/day) (17,19,22,24). In addition, little variation in iron intakes was observed between groups. As a result, differences between iron intake and status were undetectable (13).

Other factors

Vegetarian status, multivitamin use, or iron supplement use was not significantly associated with iron deficiency anemia, likely because of our small sample size. When multivitamin intake and dietary iron intake were combined, 53% of the sample met the Recommended Dietary Allowance for iron (18 mg/day). Although results were not adjusted for absorption efficiency, the use of a multivitamin still confers benefit in preventing iron deficiency anemia, thus serving as a cost-effective public health measure (7).

Food insecurity is associated with poorer health outcomes, and although no significant association was found between use of food assistance programs and iron deficiency anemia, the 61% prevalence of food insecurity in this sample was nearly triple that in single-parent households with food insecurity (22%) (15). Thus, the impact of poverty on the nutrition status of HIV-positive women cannot be understated, particularly among Aboriginal and African women.

Study limitations

Overall, iron intake and status are complex measures in persons with HIV because the disease may play a much greater role in iron absorption and metabolism than could be adjusted for in this study (8). Moreover, the limited number of ferritin measurements available (42 observations), coupled with the high variability of measurements, leaves room for random error, thus diminishing a possible association between iron intake and status. Other limitations include the small sample size, as well as the use of a diet survey that requires validation.

CONCLUSION

Women with HIV are at higher risk for iron deficiency anemia, a condition that has prevailed despite increased access to antiretroviral therapy and medical management. Necessary steps in preventing and managing iron deficiency anemia in women with HIV are routine screening (every three months), regular use of a multivitamin supplement with iron, and nutrition promotion programming that is supportive, provides helpful tools for addressing social barriers, and is culturally relevant.

RELEVANCE TO PRACTICE

As iron deficiency anemia is one of the most common deficiencies in those with HIV, dietitians can play a significant role in promoting prompt assessment, diagnosis, and treatment by helping establish protocols within interdisciplinary teams in their practice settings. These protocols may include laboratory screening for iron deficiency anemia every three months, education about and support for the use of additional iron via daily multivitamin or iron supplements, and monitoring dietary iron intake at each visit through dietary recalls. In turn, such protocols may reduce the prevalence of iron deficiency anemia by permitting therapy to be initiated earlier. Most important, dietitians can be at the forefront of preventive strategies through health promotion, which could include social marketing campaigns (raising awareness about iron deficiency anemia in those with HIV), nutrition education workshops, and group education sessions that enhance skill building, such as group cooking workshops. Finally, dietitians can advocate for patients by ensuring that programs and services in their practice settings are designed to reduce social barriers such as food insecurity. Advocacy may include taking the lead in establishing emergency food programs, community kitchens, and other community initiatives.

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