Risk-Based Questionnaires Fail to Detect Adolescent Iron Deficiency and Anemia

Deepa L. Sekhar, MD, MSc[1], Laura E. Murray-Kolb, PhD[2], Eric W. Schaefer, MS[3], and Ian M. Paul, MD, MSc[1,3]

Objective To evaluate the predictive ability of screening questionnaires to identify adolescent women at high-risk for iron deficiency or iron deficiency anemia who warrant objective laboratory testing.

Study design Cross-sectional study of 96 female individuals 12-21 years old seen at an academic medical center. Participants completed an iron deficiency risk assessment questionnaire including the 4 Bright Futures Adolescent Previsit Questionnaire anemia questions, along with depression, attention, food insecurity, and daytime sleepiness screens. Multiple linear regression controlling for age, race, and hormonal contraception use compared the predictive ability of 2 models for adolescent iron deficiency (defined as ferritin <12 mcg/L) and anemia (hemoglobin <12 g/dL). Model 1, the Bright Futures questions, was compared with model 2, which included the 4 aforementioned screens and body mass index percentile.

Results Among participants, 18% (17/96) had iron deficiency and 5% (5/96) had iron deficiency anemia. Model 1 (Bright Futures) poorly predicted ferritin and hemoglobin values (R^2 = 0.03 and 0.08, respectively). Model 2 demonstrated similarly poor predictive ability (R^2 = 0.05 and 0.06, respectively). Mean differences for depressive symptoms (0.3, 95% CI –0.2, 0.8), attention difficulty (–0.1, 95% CI –0.5, 0.4), food insecurity (0.04, 95% CI –0.5, 0.6), daytime sleepiness (0.1, 95% CI –0.1, 0.3), and body mass index percentile (–0.04, 95% CI –0.3, 0.2) were not significantly associated with ferritin in model 2. Mean differences for hemoglobin were also nonsignificant.

Conclusions Risk-based surveys poorly predict objective measures of iron status using ferritin and hemoglobin. Next steps are to establish the optimal timing for objective assessment of adolescent iron deficiency and anemia. *(J Pediatr 2017;187:194-9).*

Iron deficiency is the most common cause of anemia and in most cases it is easily treatable.[1,2] Iron deficiency and iron deficiency anemia are on a continuum such that if women deplete their iron stores with inadequate replacement (eg, heavy menstrual blood loss and a poor diet), anemia will eventually develop.[2,3] Although iron deficiency anemia affects 2%-5% of reproductive age women, over double this number, 9%-20%, are estimated to have early stage iron deficiency without anemia.[1,3,4] Symptoms of iron deficiency may include poor school performance, mood lability, fatigue, and concentration difficulty, all of which improve with iron replacement.[2,3,5-9] Iron deficiency has also been associated with food insecurity, overweight status, pica, and restless legs syndrome.[10-14]

The American Academy of Pediatrics (AAP), in partnership with Bright Futures, sets the standard for pediatric preventive care services.[15] For adolescents presenting for routine health maintenance, the Bright Futures previsit questionnaire includes 4 anemia-related questions to aid clinicians in determining risk for iron deficiency anemia.[16] If determined to be at high risk by these questions, objective laboratory testing with a hemoglobin or complete blood count (for anemia) is typically performed, with additional more costly iron studies (eg, ferritin) ordered if anemia is detected.[17,18] Although this stepwise iron deficiency risk assessment strategy is used in thousands of daily clinical encounters, this approach has several flaws: (1) hemoglobin detects anemia, but is not specific for iron deficiency anemia and may be normal in early stage iron deficiency; (2) the questionnaire's association with laboratory measures of iron status (eg, hemoglobin and ferritin) is unknown; and (3) no formalized scoring exists for the questions, which target dietary deficiencies and heavy menses (female patients only).[16-19] These iron deficiency risk factors are more applicable to older women than adolescents.[20] In addition, even though the Bright Futures questions are intended for both sexes, the prevalence of iron deficiency and iron deficiency anemia is significantly higher among female than male subjects.[3,17,18]

With this background, the study objectives were to evaluate the predictive ability of the Bright Futures previsit questions (model 1) for objective measures of iron deficiency and anemia and to compare these 4 questions with a proposed iron deficiency risk model (model 2, **Figure**, available at www.jpeds.com) based on prior

AAP	American Academy of Pediatrics
ADHD	Attention deficit hyperactivity disorder
BMI	Body mass index
PDSS	Pediatric Daytime Sleepiness Scale

From the [1]Department of Pediatrics, Penn State College of Medicine, Hershey; [2]Department of Nutritional Sciences, The Pennsylvania State University, University Park; and [3]Department of Public Health Sciences, Penn State College of Medicine, Hershey, PA

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work. Model 2 included validated screens for depression, attention deficit hyperactivity disorder (ADHD), food insecurity, and daytime sleepiness among adolescent females 12-21 years old. Our long-term goal is to provide an evidence-based recommendation to screen for iron deficiency and iron deficiency anemia among female adolescents that could be easily used in the clinical setting.

Methods

This was a cross-sectional study of female adolescents 12-21 years old enrolled from September 2015 to May 2016. Participants were enrolled during a scheduled visit to a pediatric or gynecology practice of an academic medical center. A convenience sample was continuously enrolled to meet the recruitment goal of 100 female adolescents who both completed the study questionnaire and had laboratory studies obtained. This sample size both ensured an adequate number of participants with iron deficiency and iron deficiency anemia based on national prevalence data, and was achievable with available funds. To adequately assess the predictive ability of the questionnaires, an adequate number of respondents with positive responses to the iron deficiency risk factors was required. After 50 participants with few to no positive survey responses were recruited and had laboratory studies obtained, purposive sampling was used to select adolescents with multiple positive risk factors on questionnaire completion for laboratory testing. Approval for the study and a preliminary pilot study, which assessed the appropriateness of the study questionnaire, was obtained from the Institutional Review Board of Penn State College of Medicine.

Study Questionnaire

The questionnaire included the 4 aforementioned Bright Futures Adolescent Previsit Questionnaire anemia questions: (1) Does your diet include iron-rich foods such as meat, eggs, iron-fortified cereals, or beans? (2) Have you ever been diagnosed with iron deficiency anemia? (3) Do you have excessive menstrual bleeding or other blood loss? (4) Does your period last more than 5 days?[16] In addition, the investigators developed a model of risk factors and symptoms for iron deficiency that could be assessed using validated questionnaires (**Figure**).[20]

Mood and depression symptoms were assessed via the Patient Health Questionnaire-2.[21] Concentration and attention difficulties were assessed via the adult ADHD Self-Report Scale v 1.1 Symptom Checklist. This self-report checklist has been studied for use among adolescents, and the first 6 questions (part A) may be used as a screening tool for symptoms of ADHD.[22-24] Food security was assessed via the Food Security Survey Module for Children Ages 12 Years and Older.[25] Fatigue and sleep symptoms were determined with the Pediatric Daytime Sleepiness Scale (PDSS).[26] To use the PDSS for older adolescents in the study, the first 2 questions were altered with permission as follows: (1) How often do you fall asleep or get drowsy during class periods (or at work)? and (2) How often do you get sleepy or drowsy while doing your homework (or reading)?[26] All other questionnaires were used in their original format.

Demographic data included age, race/ethnicity, and body mass index (BMI) percentile. In addition, participants were asked about whether they were currently taking hormonal contraception. Questions regarding heavy menses were included and analyzed in the Bright Futures questionnaire. However, no validated screening tool to quantify adolescent menstrual blood loss was available for inclusion in the proposed model.[16] Between April and July 2015, 2 rounds of pilot testing of the study questionnaire were completed with female adolescents, healthcare providers, and parents (total 34 participants in both rounds). Changes to the layout, design, and phrasing of questions that were not part of validated screening tools were made based on participant feedback.

Laboratory Analysis

Blood was collected at the same visit in which the study questionnaire was completed to obtain a complete blood count (includes hemoglobin), ferritin, and C-reactive protein. These tests are part of the standard recommendations by the AAP in the evaluation of a patient for iron deficiency anemia.[19,27] As mentioned above, although low hemoglobin (anemia) is most commonly due to iron deficiency anemia in adolescent females, there are other causes. However, hemoglobin may be the only objective laboratory testing ordered in the clinical setting in response to a determination of high-risk status based on a screening questionnaire. As a marker of storage iron, ferritin gives a better indication of iron status, but its comparatively higher cost and lack of available point-of-care testing results in its less frequent use if a normal hemoglobin result has been obtained.[17-19] The complete blood count was run at the clinical laboratory at Penn State Milton S. Hershey Medical Center on an automated hematology analyzer, the Sysmex XE5000, until February 2016, when this was replaced by the Sysmex XN10 (Sysmex America, Inc, Lincolnshire, Illinois). All other blood measures were conducted in a co-author's laboratory and included assays using plasma to determine ferritin (Ramco Laboratories, Inc, Safford, Texas) and C-reactive protein (Kent Laboratories, Inc, Bellingham, Washington). Healthcare providers were made aware of any laboratory results. Measurement of C-reactive protein ensured ferritin values were not artificially elevated secondary to inflammation.[27]

Statistical Analyses

We used multiple linear regression to compare model 1, the 4 Bright Futures questions, with proposed model 2, which included validated screens for depression, ADHD, food insecurity, daytime sleepiness, and BMI percentile, to levels of ferritin (mcg/L) and hemoglobin (g/dL). The distribution of ferritin was right-skewed (with a small number of very large values) and, therefore, was log-transformed prior to fitting the models. Because of their reported associations with iron deficiency and iron deficiency anemia, each model also included age, race (collapsed into other vs white; ethnicity was not included), and hormonal contraceptive use.[19,28] Adjusted R^2 was used to measure the predictive ability of each model, with higher values representing better predictions.