Assessment of iron deficiency in the context of the obesity epidemic: importance of correcting serum ferritin concentrations for inflammation\textsuperscript{1–3}

Agnès Gartner, Jacques Berger, Abdellatif Bour, Jalila El Ati, Pierre Traissac, Edwige Landais, Saâd El Kabbaj, and Francis Delperue

ABSTRACT

Background: The correction of serum ferritin (SF) concentrations for inflammation because of infectious or parasitic diseases was recently proposed, especially in developing countries, but in many countries, adiposity has become the main cause of inflammation.

Objective: We assessed, overall and by adiposity status, the bias in the estimation of iron deficiency (ID) on the basis of uncorrected SF.

Design: A cross-sectional survey in 2010 in Rabat-Salé, Morocco, used a random sample of 811 women aged 20–49 y. Adiposity was assessed by body mass index (BMI) (normal: BMI <25; overweight: BMI ≥25 to <30; obese: BMI ≥30), waist circumference, and body fat. Inflammation was indicated by a C-reactive protein (CRP) concentration >2 mg/L. ID was indicated by an SF concentration <15 μg/L. The correction factor of SF for inflammation was derived from our sample. Differential effects of SF correction on ID status on the basis of adiposity were assessed by models that included adiposity × correction interactions and accounted for the within-subject correlation.

Results: The prevalence of overweight was 33.0% and of obesity was 34.0%. Inflammation (42.3%) was strongly linked with adiposity (20.1%, 37.6%, and 68.4% in normal, overweight, and obese subjects, respectively; P < 0.0001). SF increased from a CRP concentration >2 mg/L. The correction factor of SF was 0.65. The prevalence of ID (37.2%) compared with 45.2%; difference $12.4\%$ in normal, overweight, and obese subjects, respectively; P-interaction < 0.0001). Analogous results were observed for other adiposity measures.

Conclusion: In developing countries where ID remains prevalent but rates of obesity are already high, corrected SF should be used when assessing ID status, even if infectious or parasitic diseases are no longer widespread. This trial was registered at clinicaltrials.gov as NCT01844349. Am J Clin Nutr 2013;98:821–6.

INTRODUCTION

In accordance with the latest suggestions of the WHO/CDC Technical Consultation concerning the assessment of iron status at population level (1, 2), Thurnham et al (3) recently proposed correction factors that were based on acute-phase proteins to control for the effect of subclinical inflammation on serum ferritin (SF)\textsuperscript{4} concentrations. Until now, efforts to account for inflammation when using SF to measure iron deficiency (ID) prevalence or to evaluate iron interventions focused on situations that are mainly encountered in developing countries, where both inflammation and ID were highly prevalent, and infectious or parasitic diseases or malaria were the main causes of inflammation (1, 3).

However, health conditions have evolved dramatically in the developing world. In parallel with the epidemiologic and nutrition transition, there have been improvements in health mainly because of reductions in acute infectious diseases, but at the same time, there has been an increase in noncommunicable diseases (4, 5). Specifically, many low- and middle-income countries (LMICs) already face high levels of overweight and obesity prevalence (6, 7) together with continuing high levels of ID prevalence (8), especially in women, as is the case in North Africa (5, 9). As well as being a metabolic disease, obesity can also be considered as a chronic low-grade subclinical inflammatory disease (10–15) that promotes the production of proinflammatory factors and increased concentrations of markers of inflammation in the serum, particularly C-reactive protein (CRP) (14, 16–19). These new situations have led to a shift in the main causes of inflammation. Literature on iron and inflammation emphasized that adiposity-related inflammation rendered SF concentrations less useful for the assessment of iron status (17–20) but did not propose an adjustment. Contexts in which overweight and obesity are the main causes of inflammation, contexts in which ID and inflammation are highly prevalent, and noncommunicable diseases are prevalent, and contexts where both lean and overweight individuals are affected by ID.


1 From the Institute of Research for Development (IRD), Unité Mixte de Recherche 204 (NutriPass)-IRD-Montpellier 2-Montpellier 1, Montpellier, France (AG, JB, PT, EL, and FD); the Faculty of Sciences, Ibn Tofail University, Kenitra, Morocco (AB); the National Institute of Nutrition and Food Technology, Tunis, Tunisia (JEA); and the Laboratory of Research and Medical Analyses, “Fraternelle de la Gendarmerie Royale,” Rabat, Morocco (SEK).

2 Supported by the Corus programme (financed by the French Ministry of Foreign and European Affairs) as part of the Understanding the Nutritional Transition in the Maghreb to Contribute to the Prevention of Obesity and Non-communicable Diseases project (Corus contract 6028-2).

3 Address reprint requests and correspondence to A Gartner, Nutripass, Institute of Research for Development, 911 Avenue Agropolis, 34394 Montpellier Cedex 5, France. E-mail: agnes.gartner@ird.fr.

4 Abbreviations used: BF, body fat; CRP, C-reactive protein; ID, iron deficiency; LMIC, low- and middle-income country; SF, serum ferritin; WC, waist circumference.

Received November 9, 2012. Accepted for publication June 13, 2013. First published online July 24, 2013. doi: 10.3945/ajcn.112.054551.
together with continuing high rates of ID, have not been specifically cited by WHO (1) or by Thurnham et al (3) as situations that require the correction of SF concentrations for the calculation of ID prevalence. We considered that there is an urgent need to start the use of correction factors of SF to be able to better determine iron status in obese subjects. However, we hypothesized that the correction factor proposed by Thurnham et al (3) cannot be directly used. Indeed, the amount of CRP required to shift SF concentrations may be different in the case of obesity-induced inflammation than in conditions of infection. It is needed to explore the specific correction factor from a population mainly concerned by obesity-induced inflammation.

Therefore, the objective of this work was to evaluate the effect of overall obesity-induced inflammation on SF measurement and ID prevalence in a sample of urban Moroccan women. These subjects were living in a context that is currently undergoing a nutrition transition (21) and where overweight and obesity are already highly prevalent (22, 23). With the use of a correction factor derived from our population, we compared the magnitude of the effect of the use of uncorrected SF concentrations compared with corrected concentrations in the estimation of the ID prevalence of the total sample and as a function of adiposity status.

SUBJECTS AND METHODS

Study area

Morocco is a North African lower-middle income country that has recently undergone rapid economic development. This study focused on a mainly urban area around the capital city (region of Rabat-Salé).

Design and sampling

A cross-sectional survey was carried out in 2009–2010. The target population included 20–49-y-old nonpregnant women who were living in Rabat-Salé. The survey was based on a 2-stage cluster sample of households; the sampling frame was derived from the database of the 2004 population census. A total of 45 census districts were randomly selected, and in each district, a starting point was randomly selected on a map. From each starting point, eligible households were randomly selected until 20 households with at least one woman in the 20–49-y-old age group had been identified. At the third stage, one eligible woman was randomly selected in each household.

Data and measurements

Data collection

A questionnaire was used to collect sociodemographic characteristics by interview, and anthropometric and body composition measurements were taken during home visits by specially trained personnel. Female participants were instructed to come to the Laboratory of Research and Medical Analyses in Rabat after fasting overnight to have a venous blood sample taken.

Anthropometric and body-composition measurements

Anthropometric measurements were taken according to international recommendations (24) and following standard procedures (25) to ensure accuracy. Height was measured to the nearest 0.1 cm with a stadiometer. Waist circumference (WC) was measured to the nearest 0.1 cm with a non-elastic measuring tape. Body weight was measured to the nearest 0.1 kg. Body weight and body composition were measured by using a body-composition scale (BodyUp; Tefal), which is a foot-to-foot impedance meter. Women stood barefoot on the scale. The apparatus recorded body weight, and when this was stable, predicted fat mass via the preentered subject’s age, height, and sex and the measurement of impedance from one foot to the other. The body fat (BF) mass value was read to the nearest 0.1 kg from the digital display and recorded. The percentage of BF was calculated as the ratio of fat mass to body weight. All apparatuses were checked daily. Women were classified by using BMI [in kg/m² (ie, weight divided by the square of height)] as obese (≥30) or overweight (≥25 to <30) (26). WC was used to define abdominal obesity (WC ≥88 cm) or preabdominal obesity (WC ≥80 to <88) (26). For the purpose of this study, we identified the following groups based on the percentage of BF: BF-obesity was defined as BF ≥39% in 20–39-y-old women and BF ≥41% in 40–49-y-old women, and BF-overweight was defined as BF ≥33% to <39% in 20–39-y-old women and BF ≥35% to <41% in 40–49-y-old women (27).

Iron and inflammation status

Blood samples were collected in normal tubes for SF and CRP. SF was determined by immunoassays by using an automated Coulter counter Access2 (Beckman Coulter Inc). CRP was measured by using a nephelometric procedure with a BN ProSpec system (Siemens AG). The limit of detections of CRP concentrations was 2 mg/L. Women were classified as having a normal CRP if the serum concentration was ≤2 mg/L and as having inflammation if the serum concentration was >2 mg/L. The correction factor of SF for inflammation was derived from our sample. ID was defined as an SF concentration <15 µg/L. Moreover, ID prevalence was recalculated by using corrected SF values (<15 µg/L) when inflammation was present.

Ethics

All applicable institutional and governmental regulations concerning the ethical use of human volunteers were respected during this study. The project and survey protocol were reviewed and approved by the Ethical and Deontological Consultative Committee of the Institute of Research for Development (July 2009) and by the Moroccan Ministry of Health (March 2009). After being thoroughly informed of the purpose, requirement, and procedures of the survey, all women gave their free informed consent. All data were handled anonymously during the analysis.

Data management and analysis

Data entry, including quality checks and validation by double entry of questionnaires, was performed with EpiData Software version 3.1 (28). Data management and statistical analyses were performed with the SAS system (release 9.1; SAS Institute Inc).

The type I error risk was set at 0.05 for all analyses. Results are expressed as estimates and design-based SEs or 95% CIs. The sampling design (ie, clustering and sampling weights accounting for differential probabilities of selection) (29) was taken into account in analyses.
Results

A total of 895 women were surveyed; 84 women were excluded because of a lack of biological measurements, which left a total of 811 women who were analyzed. The mean age of these women was 36.9 ± 0.4 y (Table 1). From increasing BMI, which indicated overall obesity, one-third of women presented with overweight, and more than one-third of women were obese (Table 1). From increasing WC, which indicated central obesity, one-quarter of the women presented with preadominal obesity, and >2 of 5 women presented with abdominal obesity. On the basis of the percentage of BF, one-third of women were in the BF-overweight category, and almost one-half of women were in the BF-obesity category.

On the basis of CRP concentrations >2 mg/L, inflammation concerned 42.3% (95% CI: 38.7, 45.9) of women. Whatever the adiposity indicator, the rate of inflammation in women in the normal category was never >20% (Table 2). The prevalence of inflammation increased dramatically with BMI, WC, or BF. Compared with women in the normal category, the odds of inflammation were almost 2–3 times higher in the intermediate category of adiposity; these odds increased 9-fold in obese women, 8-fold in women with abdominal obesity, and 7-fold in women with BF-obesity (Table 2).

When we assessed the relation between CRP and SF, the SF geometric mean was calculated in 3 subsets according to the CRP concentration cutoffs of 2 mg/L (the cutoff in the current study) and 5 mg/L [the cutoff used by Thurnham et al (3)]. SF geometric mean concentrations were 16.3, 24.5, and 25.6 mg/L in women with CRP concentrations ≤2 mg/L (n = 463), 2–5 mg/L (n = 127), and >5 mg/L (n = 221), respectively. SF concentrations increased from CRP concentrations >2 mg/L.

We determined the relative difference in the mean SF concentration (ratio of geometric means) in women who had inflammation or not. The geometric mean SF concentration was 54% higher when CRP concentrations were >2 mg/L (25.2 μg/L) than ≤2 mg/L (16.3 μg/L). This difference converts to a multiplier of 0.65 when we applied to reduce SF concentrations when CRP concentrations were >2 mg/L, in order to remove the influence of adiposity-induced inflammation from SF concentrations. In the whole sample of women, the geometric mean value of SF concentrations was 18.9 ± 1.0 μg/L before correction (Table 1) and 15.7 ± 1.0 μg/L after correction (data not shown).

Overall, the ID prevalence on the basis of not-corrected SF was lower than that on the basis of corrected SF [37.2% (95% CI: 33.4%, 41.0%) compared with 45.2% (95% CI: 41.1%, 49.3%); i.e, a difference of −8.0%; P < 0.0001] (Table 3). When we detailed the extent of underreporting of ID by levels of adiposity, BMI, WC, and SF, each variable displayed a strong interaction with SF correction (all P < 0.0001) because differences in prevalence (not-corrected compared with corrected SF) increased dramatically with the level of adiposity. Differences were quite small in the lowest category of adiposity (normal women; i.e, −2.9% for BMI, −2.5% for WC, and −2.7% for BF); differences were greater in the intermediate category and even greater in women who presented with high adiposity (−12.4%, −10.6%, and −12.0% for BMI, WC, and BF, respectively) (Table 3).

Discussion

When calculated by using our adjustment to deal with the effect of inflammation on SF concentrations and on the basis of a large random sample, the estimated prevalence of ID in a population of Moroccan women of reproductive age was as high as 45.2%. The estimated prevalence on the basis of not-corrected SF underestimated ID by −8.0%, which corresponded to a rate of underestimation of 17%. This rate was close to the underestimation

### TABLE 1

Data from nonpregnant women in the Rabat-Sale region, Morocco (n = 811)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>36.9 ± 0.4&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>158.9 ± 0.3</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>69.9 ± 0.7</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.7 ± 0.2</td>
</tr>
<tr>
<td>Overweight (25 to &lt;30 kg/m²) (%)</td>
<td>33.0 (29.6, 36.5)&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td>Obesity (≥30 kg/m²) (%)</td>
<td>34.0 (29.8, 38.2)</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>86.5 ± 0.6</td>
</tr>
<tr>
<td>Preadominal obesity (waist circumference ≥80 to &lt;88 cm) (%)</td>
<td>25.4 (21.6, 29.4)</td>
</tr>
<tr>
<td>Abdominal obesity (waist circumference ≥88 cm) (%)</td>
<td>43.3 (39.0, 47.5)</td>
</tr>
<tr>
<td>Percentage of BF&lt;sup&gt;4&lt;/sup&gt;</td>
<td>38.8 ± 0.3</td>
</tr>
<tr>
<td>BF-overweight (%)</td>
<td>33.9 (30.5, 37.4)</td>
</tr>
<tr>
<td>BF-obesity (%)</td>
<td>46.3 (41.9, 50.8)</td>
</tr>
<tr>
<td>C-reactive protein geometric mean (mg/L)</td>
<td>3.5 ± 1.0</td>
</tr>
<tr>
<td>Serum ferritin geometric mean (μg/L)</td>
<td>18.9 ± 1.0</td>
</tr>
</tbody>
</table>

<sup>1</sup> Cluster sampling and sample weight were used for all analyses. BF, body fat.

<sup>2</sup> Mean ± SEM (all such values).

<sup>3</sup> Prevalence; 95% CI in parentheses (all such values).

<sup>4</sup> BF-obesity was defined as BF ≥39% in 20–39-y-old women and BF ≥41% in 40–49-y-old women, and BF-overweight was defined as BF ≥53% to <39% in 20–39 y old women and BF ≥35% to <41% in 40–49-y-old women.
The current study showed that the concentration of CRP required to shift SF concentrations was >2 mg/L. This concentration is a lower cutoff than that (>5 mg/L) used to derive the factor recently reported to correct SF in individuals from low-income countries in whom the inflammation was mainly a result of infections (3). When derived from our population, the correction factor was 0.65, which is the same value as the value of the correction factor published by Thurnham et al (3).

As previously stated, the usefulness of adjusting SF concentrations to account for inflammation in the estimation of ID prevalence has already been analyzed and proposed in the context of malaria and other situations of endemic infectious or parasitic diseases (1–3, 32, 33). But the most recent WHO recommendations (1, 2) still discussed infectious or parasitic diseases or malaria as the only causes of inflammation without citing overweight or an excess of BF as a condition that may account for inflammation and, hence, implying the need to correct SF concentrations. To our knowledge, this is the first study to investigate the effect of obesity-induced inflammation on the determination of iron status by using SF. We showed that the adjustment of SF is also needed and applicable in new situations in which the causes of inflammation are linked to increased adiposity. What is important is that SF data are corrected for inflammation to provide a more accurate estimate of ID prevalence in a given population, making correction for inflammation essential when ID is compared between areas or countries in which the prevalence of obesity may differ (in other words, between countries at different stages of the nutrition transition). The variability of ID prevalence depending on the use of uncorrected or corrected SF concentrations may be important in public health terms because the global effect of the adjustment had been linked to the prevalence of overweight or obesity in the population. It had been predicted that the annual number of deaths as a result of chronic diseases will increase in the next 20 y, whereas deaths as a result of infectious diseases are expected to decline (34). Current projections have indicated that, by 2020, the highest increases in mortality because of noncommunicable diseases will take place in Africa and other LMICs (35). Consequently, the measurement of inflammation indicators and adjustment of values of SF (and probably of other blood indicators

TABLE 2
Association of inflammation with BMI, waist circumference, or percentage of BF in 20–49-y-old nonpregnant women in Rabat-Salé (n = 811)†

<table>
<thead>
<tr>
<th>BMI</th>
<th>n</th>
<th>Prevalence (%)</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal: &lt;25 kg/m²</td>
<td>256</td>
<td>20.1</td>
<td>1 (—)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Overweight: 25 to &lt;30 kg/m²</td>
<td>276</td>
<td>37.6</td>
<td>2.4 (1.7, 3.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Obesity: ≥30 kg/m²</td>
<td>279</td>
<td>68.4</td>
<td>8.6 (5.7, 13.0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Waist circumference</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal: &lt;80 cm</td>
<td>244</td>
<td>18.0</td>
<td>1 (—)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Preabdominal obesity: 80 to &lt;88 cm</td>
<td>209</td>
<td>37.4</td>
<td>2.7 (1.6, 4.5)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Abdominal obesity: ≥88 cm</td>
<td>358</td>
<td>62.7</td>
<td>7.7 (4.8, 12.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Percentage of BF</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal: 33%/35%</td>
<td>143</td>
<td>18.8</td>
<td>1 (—)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BF-overweight: 33%/35% to &lt;39%/41%</td>
<td>282</td>
<td>28.8</td>
<td>1.8 (1.1, 2.8)</td>
<td>0.021</td>
</tr>
<tr>
<td>BF-obesity: ≥39%/41%</td>
<td>386</td>
<td>62.2</td>
<td>7.1 (4.4, 11.6)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

† Cluster sampling and sample weight were used for all analyses (logistic regression). BF, body fat.
‡ Defined as a C-reactive protein concentration >2 mg/L.
§ Defined as 33% in 20–39-y-old women and 35% in 40–49-y-old women.
¶ Defined as 39% in 20–39-y-old women and 41% in 40–49-y-old women.

(14%) reported by Thurnham et al (3) in situations in which inflammation was mainly a result of infectious or parasitic diseases or malaria. The correction of SF concentrations avoided a significant underestimation of ID in our population. More importantly, the correction prevented the exclusion of individuals with inflammation. The exclusion of these individuals was previously recommended (32) but was considered to be impractical when the prevalence of inflammation was high, such as in our population in which almost 1 of 2 women presented with elevated CRP. The correction we applied appeared to be appropriate because we obtained a prevalence of ID of 45.2% in our population, which was similar to the prevalence of ID in the subgroup of women without inflammation (44.3%).

In our study context, the high prevalence of inflammation was very likely mainly a result of adiposity because almost all elevated CRP was associated with increased overall or central adiposity. Indeed, almost 9 of 10 women who presented with inflammation also presented with increased adiposity (84.4% with overweight or obesity, 86.7% with preabdominal or abdominal obesity, and 91.2% with SF-overweight or SF-obesity) (data not shown). As expected, the rate of elevated CRP increased with an increase in BMI. Rates of CRP concentrations >10.0 mg/L in women in the 3 BMI categories in our study [ie, 3.5%, 9.6%, and 17.9% (data not shown)] were very similar to those reported in the United States aged ≥17 y from the NHANES III (ie, 4.0%, 7.7%, and 20.2%, respectively) (16); rates of CRP concentrations >2 mg/L in the 3 BMI categories in our study also resembled those from the NHANES III. Moreover, we showed that the rate of inflammation also increased with elevated WC or BF, which are 2 other indicators of adiposity that, if they are too high, point to inflammation (14). In women who presented with adiposity (an elevated BMI, WC, or percentage of BF), approximately one-half of them also presented with inflammation. Moreover, the OR of inflammation in the BMI, WC, or BF highest group was >7 compared that in the normal BMI, normal WC, or normal BF group.

The current study showed that the concentration of CRP required to shift SF concentrations was >2 mg/L. This correction is a lower cutoff than that (>5 mg/L) used to derive the factor recently reported to correct SF in individuals from low-income countries in whom the inflammation was mainly a result of infections (3). When derived from our population, the correction factor was 0.65, which is the same value as the value of the correction factor published by Thurnham et al (3).
Corrrecting serum ferritin when obese

**TABLE 3**

Modifying effect of adiposity (BMI, waist circumference, or percentage of BF) on serum ferritin correction to estimate the prevalence of iron deficiency in 20-49-y-old nonpregnant women in Rabat-Salé, Morocco (*n* = 811)

<table>
<thead>
<tr>
<th></th>
<th>Prevalence (%)</th>
<th>Difference in prevalence (not-corrected compared with corrected SF)</th>
<th>Estimated percentage (95% CI)</th>
<th><em>P</em></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Not corrected</td>
<td>SF corrected</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>37.2</td>
<td>45.2</td>
<td>−8.0 (−9.9, −6.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal: &lt;25 kg/m²</td>
<td>256</td>
<td>43.9</td>
<td>−2.9 (−4.7, −1.2)</td>
<td>0.0009</td>
</tr>
<tr>
<td>Overweight: 25 to &lt;30 kg/m²</td>
<td>276</td>
<td>36.5</td>
<td>−8.5 (−12.0, −5.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Obesity: ≥30 kg/m²</td>
<td>279</td>
<td>31.3</td>
<td>−12.4 (−16.6, −8.3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>WC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal: &lt;80 cm</td>
<td>244</td>
<td>45.6</td>
<td>−2.5 (−4.2, −0.9)</td>
<td>0.0027</td>
</tr>
<tr>
<td>Preabdominal obesity: 80 to &lt;88 cm</td>
<td>209</td>
<td>35.6</td>
<td>−10.4 (−14.5, −6.3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Abdominal obesity: ≥88 cm</td>
<td>358</td>
<td>32.0</td>
<td>−10.6 (−14.0, −7.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BF</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal: &lt;33%/35%</td>
<td>143</td>
<td>46.0</td>
<td>−2.7 (−4.8, −0.5)</td>
<td>0.015</td>
</tr>
<tr>
<td>BF-overweight: 33%/35% to &lt;39%/41%</td>
<td>282</td>
<td>39.0</td>
<td>−5.7 (−8.6, −2.8)</td>
<td>0.0001</td>
</tr>
<tr>
<td>BF-obesity: ≥39%/41%</td>
<td>386</td>
<td>32.1</td>
<td>−12.0 (−15.4, −8.6)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

1 BF, body fat; SF, serum ferritin; WC, waist circumference.
2 Weighted estimates.
3 *P*-interaction values: the null hypothesis of identical uncorrected compared with corrected difference in iron-deficiency prevalence in all 3 adiposity categories (identity-binomial generalized linear model by using generalized linear estimating equations to account for the within-subject correlation when the 2 assessments of iron deficiency on the same subjects were compared).
4 BMI × SF correction.
5 WC × SF correction.
6 Percentage of BF × SF correction.
7 Defined as 33% in 20–39-y-old women and 35% in 40–49-y-old women.
8 Defined as 39% in 20–39-y-old women and 41% in 40–49-y-old women.

### Table 3: Modifying effect of adiposity (BMI, waist circumference, or percentage of BF) on serum ferritin correction to estimate the prevalence of iron deficiency in 20-49-y-old nonpregnant women in Rabat-Salé, Morocco (*n* = 811)

<table>
<thead>
<tr>
<th></th>
<th>Prevalence (%)</th>
<th>Difference in prevalence (not-corrected compared with corrected SF)</th>
<th>Estimated percentage (95% CI)</th>
<th><em>P</em></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Not corrected</td>
<td>SF corrected</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>37.2</td>
<td>45.2</td>
<td>−8.0 (−9.9, −6.1)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Iron deficiency may be affected by inflammation (such as serum retinol) will be particularly important in populations like the one in the current study in which more than two-thirds of the women sampled were overweight or obese. Beyond urban Morocco, such a high prevalence of overweight has already been observed in many LMICs (7, 36), especially in North Africa and the Middle East (36, 37). This adjustment could be even more crucial in the near future, because, if recent trends continue, by 2030, 3.3 billion adults worldwide could be either preobese or obese, with 80% of them being from an LMIC (36, 38).

Relative to the number of ID cases obtained with the corrected SF, unidentified cases of ID on the basis of uncorrected SF represented false negatives. When calculated as a ratio of the number of actual ID cases assessed after ID adjustment, false-negative cases were only 6.2% in normal-BMI women, 5.2% in normal-WC women, and 5.5% in normal-BF women. In contrast, in women who presented with obesity, abdominal obesity or BF-obesity, the proportion of false negatives reached 28.3%, 24.9%, and 27.2%, respectively. These results meant that 1 of 4 women with ID would not have been detected without adjustment of the SF concentration if she had overall or central or BF-obesity. Beyond the estimation of ID prevalence at the regional or national level, the aim of epidemiologic studies pertaining to ID is also often to estimate its relations at subject level with associated factors such as socioeconomic or lifestyle factors; thus, not correcting individual ID status for inflammation would also risk biasing associations, all the more for factors strongly correlated with obesity.

One strength of this study was that it was based on a large, random sample of women from an urban area in Morocco; indeed, this is a typical nutrition transition context in LMICs where the issue of correcting prevalence of ID for inflammation because of obesity is particularly important. One limitation of the study could have been that, for reasons of cost and practicality, only 1 of 2 acute-phase proteins recommended for the adjustment of SF concentration (3) was used, which allowed only the identification of subjects with acute or current inflammation but not subjects in the convalescence phase. However, the aim of the study by Thurnham et al (3) was to characterize inflammation because of infectious or parasitic diseases or malaria, whereas the aim of the current study was to define adiposity-induced inflammation in noninfectious subjects with other subjects, the analyses enabled the estimation of a coherent gradient in the relation between differences in the prevalence of ID (corrected compared with not-corrected SF) and the level of adiposity.

In conclusion, in a population of urban Moroccan women typical of a context of nutrition transition, we have shown that a significant underestimation of the prevalence of ID was caused...
by not using a correction factor (by using CRP as the marker of inflammation). In LMICs where ID remains prevalent along with already high rates of overweight and obesity, inflammation-related adiposity is an important new reason to adjust SF concentrations to correct for effects of inflammation; this adjustment is needed even if infectious or parasitic diseases are no longer widespread because of the shift in the burden of disease related to the epidemiologic transition. In these contexts, when the prevalence of ID is measured, associated factors are assessed, or iron interventions with a single indicator are evaluated, ID status corrected for inflammation should be used.

In addition to the authors, the other members of the Understanding the Nutritional Transition in the Maghreb to Contribute to the Prevention of Obesity and Non-communicable Diseases Study Group in Morocco were as follows: H Aguenaou, H Belghiti, O Ayyat, N Choua, N Derbali, HEI Haiani, S Goumi, and N Mokhtar (University Ibn Tofail, Kenitra, Morocco); K El Kari and M El Mizbi (Cnesten, Rabat, Morocco); A Derouiche (University Ben M’sink, Casablanca, Morocco); Y Kameli, B Maire, and M Holdsworth (Institute for Research for Development (IRD), Unité Mixte de Recherche Nutripass IRD-University of Montpellier-1-University of Montpellier-2, Montpellier, France); and M Holdsworth (Division of Nutritional Sciences, University of Nottingham, United Kingdom.

The authors’ responsibilities were as follows—AG, JB, AB, JEA, and FD: designed the research; AG, JB, EL, and FD: conducted the research; SEK: analyzed data and performed the statistical analysis; AG, JB, PT, and FD: wrote the manuscript; AG: had primary responsibility for the final content of the manuscript; and all authors: read and approved the final manuscript. None of the authors had a conflict of interest.

REFERENCES

15. Bastard JP, Maachi M, Lagathu C, Kim MJ, Caron M, Vidal H, Capeau J, Feve B. Recent advances in the relationship between obesity, inflammation, and insulin resistance. Eur Cytokine Netw 2006;17:4–12.