Iron Deficiency in Adolescent Female Athletes—Is Iron Status Affected by Regular Sporting Activity?

Göran Sandström, MD,* Mats Börjesson, MD, PhD,† and Stig Rödjer, MD, PhD‡

Objective: To determine the prevalence of iron deficiency (ID) and iron deficiency anemia (IDA) among a group of female athletes and compare with an age-matched group of female nonathletes. To study lifestyle factors that could play a role in the development of ID and IDA and compare these factors between the groups.

Design: A controlled clinical trial.

Setting: A senior high school for athletes in Gothenburg, Sweden.

Participants: All female athletes at a senior high school for top-level athletes were offered to take part. Fifty-seven female athletes accepted to participate in the study. The control group consisted of a random sample of 130 age-matched nonathlete students; 92 accepted to participate in the study.

Intervention: Intervention was not an actual part of this study but those with ID and IDA were treated with iron by the regular school doctor.

Main Outcome Measures: Iron deficiency anemia and ID were determined by levels of hemoglobin, serum iron, total iron-binding capacity, transferrin saturation, and serum ferritin.

Results: The main result of the study is the finding that ID and IDA are common among young adolescent female athletes and that there was no difference between female athletes and nonathletes. In the athlete group, 30 of 57 individuals (52%) had ID compared with 43 of 92 individuals (48%) in the nonathlete group (P > 0.3). Comparisons of the 2 groups showed no significant difference in hemoglobin (P > 0.30). In total, we found that 5 of 57 athletes (8.6%) had IDA compared with 3 of 92 nonathletes (3.3%), the difference being not statistically significant (P = 0.24).

Conclusions: The main finding of this study is that ID and IDA are common among female adolescents but not more common among athletes than nonathletes. The results are despite factors that should favor a better iron status in the athlete group, such as better iron intake and less menstrual bleeding. Other factors that might have an impact on iron balance, must therefore be considered.

Key Words: iron, iron deficiency, iron deficiency anemia, female athletes, lifestyle factors, acute phase response


INTRODUCTION

Iron deficiency (ID) affects a great number of people, almost 50% of the population worldwide,† making it the most common nutritional deficiency of all.‡ Iron deficiency anemia (IDA) is the end state of ID, and there is a clear gender difference, with ID being most prevalent among women.§

The relation between ID and physical activity has been widely studied because IDA also affects female athletes.¶ There are varying results regarding iron status among female athletes. Some report that team athletes have better iron status than controls,¶¶ one study reported no difference,¶¶¶ while other studies showed that athletes were more iron depleted than nonathlete women.¶¶¶ In a pilot study of elite female soccer players,¶¶¶¶ we found that 55% of the players were iron depleted, which was higher than expected compared with the known prevalence figures in nonathletes.¶¶¶¶ However, it is still not clear if female athletes have a higher prevalence of ID and IDA than age-matched controls.

Although also widely studied, the effect of ID, without anemia, on athletic performance is not clear.¶¶¶¶ Theoretically, reduction in oxygen-carrying capacity impairs aerobic capacity, whereas reduction in tissue oxidative capacity impairs endurance and energetic efficiency.¶¶¶¶¶ It is clear that established IDA per se causes a reduced aerobic capacity (for hemoglobin values up to 200 g/L)¶¶¶¶ and that a reduced exercise capacity in turn affects the maximal performance capacity of a top-level athlete.¶¶¶¶¶

The combination of inadequate dietary intake and primarily losses by menses is thought to be the main cause of ID.¶¶¶¶ In addition, it has been suggested that physical activity itself could be a cause for ID and even IDA. A subnormal hemoglobin concentration has also been reported in athletes and has been termed “sports anemia.”¶¶¶¶¶ Different mechanisms have been proposed, for example, pseudo-dilution, increased iron losses through sweating, intravascular mechanical hemolysis, to mention a few.¶¶¶¶¶ The role of age in the development of ID and IDA is interesting. The true prevalence of ID and IDA in adolescent female athletes compared with nonathletes is not known. Furthermore, the mechanisms for ID in these groups of young female athletes are not fully

Submitted for publication January 17, 2012; accepted June 7, 2012.

From the *Department of Anesthesiology and Intensive Care, Sahlgrenska University Hospital, Gothenburg, Sweden; †Department of Acute and Cardiovascular Medicine, Sahlgrenska University Hospital, Gothenburg, Sweden; and ‡Section of Hematology and Coagulation, Department of Medicine, Sahlgrenska University Hospital, Gothenburg, Sweden. Supported by grants from The Swedish National Centre for Research in Sports and The Göteborg Medical Society.

The authors report no conflicts of interest.

Corresponding Author: Göran Sandström, MD, Department of Anesthesiology and Intensive Care, Sahlgrenska University Hospital, Smörsllottsgatan 1, SE 416 85 Gothenburg, Sweden (goran.sandstrom@gu.se).

Copyright © 2012 by Lippincott Williams & Wilkins.

elucidated. We have previously shown that ID and IDA were common among slightly older soccer players (19-28 years) at the highest elite level.

The main purpose of the study was to find out if physical activity at elite level affects iron status. Therefore, we wanted to determine the prevalence of ID and IDA among a group of adolescent female athletes younger than the national team players and compare with an age-matched group of nonathletic females. We also wanted to study lifestyle factors that could play a role in the development of ID and IDA and compare these factors between the groups.

**METHODS**

To study the prevalence of ID and IDA in young adolescent female athletes and comparable nonathletes, we conducted a controlled study consisting of a survey and standard blood samples, in a school in Gothenburg, Sweden, attended by these 2 groups of young women.

**Subjects**

All female student athletes (n = 71) at a senior high school for top-level athletes were offered to participate in the investigation. This specific school is a senior high school for top student athletes recruited partly from the local area and partly from all over Sweden. They practice different sports, both individual and team sports. With the assistance of a statistician, a control group consisting of a random sample of the nonathlete students was offered to take part in the investigation. To minimize dropouts, we offered the participants 3 possible times for testing.

Finally, a total of 149 healthy young female participants [81% of athletes (n = 57) and 71% of controls (n = 92)], 15 to 19 years old, took part in the investigation. The reasons for declining to participate in the study were mainly nervousness for the blood test itself, whereas a few individuals <18 years of age did not get permission from their parents to participate.

Exclusion criteria were pregnancy, ongoing infection, and a history of hematological disease (except for IDA). None of the athletes or the controls fulfilled the exclusion criteria.

**Regular Physical Activity Level**

The female athletes recruited were all active in their sport at a high national level corresponding to their age, and they were practicing 4 to 6 h/wk (mean, 5 hours) at school. In addition, they practiced 4 to 6 times per week in their clubs (duration of 60-90 minutes each time). Each subject had to specify their sport; 86% of all were engaged in ball sports: handball 44%, soccer 30%, tennis 9%, and golf 3%. The remaining athletes (14%) were active in swimming (7%), wrestling (5%), and figure skating (2%). In the control group, no subject was active in any sport outside school, and in school they were physically active less than 2 h/wk.

**Basal Characteristics and Questionnaire**

All participants filled in a questionnaire in the same session as when the blood samples were drawn. This questionnaire consisted of questions on family history (hereditary disease), smoking habits, and dietary habits covering number of meals per day and if they were eating breakfast or not. The questionnaire also included items on specific food intake, such as meat, coffee, tea, dietary supplements, and medications, including hormonal contraceptives. In addition, there were questions about eating pattern, active weight loss, and if they were trying to gain weight. The subject had to specify the menstrual bleeding as: 1 = sparse, 2 = normal, and 3 = abundant. Body mass index (BMI) was calculated from the weight (in kilograms) divided by the square of the height (in meters).

**Blood Samples**

The venous blood samples for evaluation of ID and IDA covered hemoglobin, serum iron, total iron-binding capacity (TIBC), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC). These were drawn at the clinic at the school on certain given times. The subjects had not undertaken any training on the day before the blood sampling.

All subjects were fasting from midnight, and venous blood samples were drawn between 10 and 12 AM, with the subjects in a semisupine position. The concentration of hemoglobin (Hb), the erythrocyte indices (MCV, MCH, and MCHC), and erythrocyte particular concentration was determined the same day. Serum was kept frozen at −70°C, and analysis of serum iron (Fe), TIBC, and serum ferritin was performed according to standard laboratory procedures. The concentration of hemoglobin was determined by the Technicon H2 method (Bayer Diagnostics, Tarrytown, New York). Serum iron was determined with a photometric method as a ferrozine complex on Hitachi 917 (Boehringer Mannheim, Indianapolis, Indiana). Total iron-binding capacity was calculated from measurements of serum transferrin with an immunochrometic method on Hitachi 917. Transferrin saturation (TS) was the ratio of serum iron to TIBC expressed as a percentage. Serum ferritin was measured by an immunochrometic method using a mouse monoclonal antiferritin antibody and determined by alkaline phosphate conjugation according to AxSYM system (Abbott Laboratories, Abbott Park, Illinois). The values of MCV, MCH, and MCHC were measured on a CellDyn 400 (Abbott Laboratories) by cytometric method of particle count.

The following definitions were used: anemia—hemoglobin (Hb) <120 g/L before substitution was diagnosed as absolute anemia according to the World Health Organization’s definition. A rise of 10 g/L or more within the reference interval on iron supplementation was considered as relative anemia; iron deficiency—serum ferritin <16 μg/L was defined as certain ID, if Hb >120 g/L.

**Follow-up and Iron Substitution**

The individuals in the group of female athletes with ID and IDA were treated with iron supplementation (ferrous succinate 37 mg Fe/tablet, 2 tablets 2 times a day) for 3 months with a follow-up of the blood tests. This was not done as a part of the study. The female nonathletes with ID and IDA were treated as well with iron supplementation. The individuals with IDA, from both groups, were referred to the regular school doctor for further clinical follow-up.

---

Sandström et al. Clin J Sport Med • Volume 22, Number 6, November 2012

© 2012 Lippincott Williams & Wilkins

496 | www.cjsportmed.com
Statistical Analysis
We used commercially available statistical software (SPSS 16.0; SPSS, Inc, Chicago, Illinois) to perform statistical analysis. Descriptive statistics are presented as mean ± SD or range. For comparisons of demographic characteristics, we used Student t test and χ² test. All tests were 2 sided. P < 0.050 was considered statistically significant. Comparisons between variables were performed with Pitman test.

Ethical Committee
This study was approved by the Ethics Committee at Sahlgrenska Academy at Gothenburg University (application no.: 2000:Ö005). The subjects participating gave their verbal informed consent to take part in the investigation. For those younger than 18 years, the parents were asked for approval. The methods used in this investigation were in accordance with the Helsinki Declaration of 1975 as revised in 1983.

RESULTS
Baseline Characteristics
All figures on basic characteristics for participation in the investigation are shown in Table 1. The mean age was 17 years in both groups (range, 15-18 years in athletes and 15-19 years in nonathletes, respectively). There was no significant difference in weight between the 2 study groups, but there was a tendency that the athletes were slightly heavier, with a mean weight of 64 ± 6 kg (range, 52-78 kg), compared with the nonathletes, with a mean weight of 61 ± 10 kg (range, 45-105 kg) (P = 0.068). There was no significant difference in height between the 2 groups. The mean height in the study group was 1.68 ± 0.07 m (range, 1.50-1.90 m) compared with 1.66 ± 0.06 m (range, 1.50-1.80 m) in the control group. The calculated BMI was similar, being 22.5 ± 1.8 kg/m² (range, 19-27 kg/m²) in the athlete group and 21.9 ± 3.4 kg/m² (range, 17-39 kg/m²) in the nonathlete group (not significant).

Iron Deficiency Status
All figures on iron status are shown in Table 2. In the athlete group, 30 of 57 individuals (52%) had ID compared with 43 of 92 individuals (48%) in the nonathlete group (P > 0.3). There was no difference in ferritin in the athletes compared with the nonathletes (P > 0.3). However, there was a significant difference between the 2 groups in serum iron (P < 0.004), being 14 ± 6 μmol/L in the study group and 17 ± 7 μmol/L in the control group, TIBC (P = 0.018), being 73 ± 11 μmol/L in the athlete group and 78 ± 12 μmol/L in the nonathlete group, but not in TS (P = 0.069).

Anemia
Comparisons of the 2 groups showed no significant difference in hemoglobin (P > 0.30), with results showing a mean value of 136 ± 9 g/L in the study group and 138 ± 9 g/L in the control group (Table 2). There was no difference in erythrocyte particle concentration for the athlete group compared with the nonathlete group. There was no difference in MCV (P = 0.19) for the athlete group and the nonathlete group.

In total, we found that 5 of 57 athletes (8.6%) had IDA compared with 3 of 92 nonathletes (3.3%), the difference being not statistically significant (P = 0.24). Among the 5 athletes with anemia, 2 had certain IDA with hemoglobin <120 g/L and 3 had a relative anemia, that is, their hemoglobin value increased with more than 10 g/L after iron supplementation. In the nonathlete group, all subjects with IDA had certain IDA, according to the definition in the Methods section.

Dietary Habits
The young female athletes more often than the nonathlete women reported eating breakfast, 81% of the athletes compared with 52% of the nonathletes (P < 0.001). They also reported a significantly higher consumption of milk, with 75% of the athletes reporting drinking milk every day compared with 52% of the nonathletes (P = 0.007). In addition, the athletes ate more often as shown by the number of reported meals per day: 3.4 ± 0.6 for the athletes and 3.0 ± 0.9 for the nonathletes (P = 0.003). In the nonathlete group, there was a significant correlation between the number of meals and the level of ferritin (P = 0.02). This correlation was not significant in the athlete group. There was no significant difference between the groups in the use of dietary supplements (P = 0.06) or in the consumption of coffee (P = 0.21), tea (P = 0.27), or meat (P = 0.06) (Table 3).

Additional Lifestyle Factors
The nonathlete women were smokers at a greater extent than the athletes (27% and 9% respectively, P = 0.009). Female athletes did not practice active weight loss as often as nonathletes (42% compared with 63%, P = 0.02).

The female athletes reported less menstruation (1.9 ± 0.5 compared with 2.1 ± 0.5 in the nonathlete group, P = 0.02) calculated from the answers in the questionnaire (see Methods).

The time of menarche was not significantly different, being 12.6 ± 1 years (range, 9-15 years) for the female athletes and 12.4 ± 1 years (range, 10-15 years) for the nonathletes (P < 0.30), respectively. The female athletes also

<table>
<thead>
<tr>
<th>TABLE 1. Basic Characteristics for the Female Adolescents Participating in the Investigation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Characteristics</strong></td>
</tr>
<tr>
<td><strong>Mean ± SD</strong></td>
</tr>
<tr>
<td>Age, y</td>
</tr>
<tr>
<td>Height, m</td>
</tr>
<tr>
<td>Weight, kg</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
</tr>
</tbody>
</table>

© 2012 Lippincott Williams & Wilkins www.cjsportmed.com | 497
As earlier reported, ID and IDA are also very common among young adolescent female athletes and that there was no difference between female athletes and nonathletes. This finding is not unexpected because ID and IDA are common conditions in women worldwide in this regard.\(^{3}\) As earlier reported, ID and IDA are also very common in female athletes.\(^{5,9,10}\) In this study, we found that ID and IDA also are common among the younger adolescent female athletes, 52% had ID and 9% had IDA.

A possible limitation of this study might be that the definition of an athlete might be a subject for discussion. Traditionally, many investigators look at an athlete as a track and field athlete, and especially long distance runners have been subjects in many studies in the field of ID and IDA. In our study, almost 90% were active in ball sports.

Table 3 shows the lifestyle factors of athletes and nonathletes. In the present study but that was not statistically significant. In the study by Di Santolo et al.,\(^{22}\) they also found a higher proportion of athletes with IDA than in our study. This could be because we studied young adolescent female athletes compared with the older female athletes in the Italian study.\(^{22}\) In other studies, the study subjects have been older and therefore might have developed IDA at a higher extent because of a longer period of ID related to an inadequate iron intake and losses by menses as discussed above for nonathletes. Thus, the low number of years menstruating may possibly explain the nonsignificant difference compared with nonathletes.

It is known that serum iron decreases during active training, and this is probably due to the inflammatory response of physical activity.\(^{12}\) Physical exercise starts an acute-phase response leading to postexercise levels of cytokines comparable with those seen in severe burns, inflammatory disease, or bacterial infections.\(^{23,24}\) Intense physical training can induce a 2- to 3-fold increase in pro-inflammatory cytokine levels of tumor necrosis factor-\(\alpha\) and interleukin (IL)-1\(\beta\),\(^{25}\) and also the cytokine IL-6.\(^{26}\) The increase in

<table>
<thead>
<tr>
<th>Measure</th>
<th>Athletes (n = 57)</th>
<th>Nonathletes (n = 92)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb, g/L</td>
<td>138 ± 9.0</td>
<td>118–157</td>
<td></td>
</tr>
<tr>
<td>MCV, fl</td>
<td>90.0 ± 4.44</td>
<td>74–100</td>
<td></td>
</tr>
<tr>
<td>RBC, 10(^{12})/L</td>
<td>4.6 ± 0.27</td>
<td>4.0–5.2</td>
<td></td>
</tr>
<tr>
<td>S-Fe, μmol/L</td>
<td>14.0 ± 6.00</td>
<td>4.0–36.0</td>
<td></td>
</tr>
<tr>
<td>TIBC, μmol/L</td>
<td>73.3 ± 10.7</td>
<td>49–100</td>
<td></td>
</tr>
<tr>
<td>TS, %</td>
<td>19.5 ± 8.4</td>
<td>4.0–47.0</td>
<td></td>
</tr>
<tr>
<td>Ferritin, μg/L</td>
<td>21 ± 13.8</td>
<td>3.0–63.0</td>
<td></td>
</tr>
</tbody>
</table>

In 1994, 8 years before our study started, a population-based study was done in Gothenburg to investigate the iron status for girls of 15 to 16 years of age.\(^{20}\) The authors found the mean hemoglobin concentration to be 136 g/L, which is the same as in our study. They reported that 36% had ID and 7% had IDA. The level of ID seems to be lower than that in our study. The question is why? One explanation could be the fact that a larger part of the subjects in our study was older than 16 years. Recently, a study on iron status in European adolescents has been presented. In this study of girls aged 12.5 to 17.5 years, they found that the mean value of hemoglobin was 138 g/L, 21% had iron depletion defined as ferritin ≤15 μg/L corresponding to our definition of ID,\(^{21}\) showing an even lower prevalence of ID in a younger nonathletic population.

There was no difference between athletes and nonathletes in our study regarding hemoglobin value and iron status, defined as TS and ferritin, which are the common markers of iron status. However, the mean levels of serum iron and TIBC were significantly lower in the athlete group. Di Santolo et al.\(^{22}\) reported that female athletes had lower serum iron and TS but no difference in transferrin and ferritin. There was a tendency for lower TS in the athlete group in the present study but that was not statistically significant. In the study by Di Santolo et al.,\(^{22}\) they also found a higher proportion of athletes with IDA than in our study. This could be because we studied young adolescent female athletes compared with the older female athletes in the Italian study.\(^{22}\) In other studies, the study subjects have been older and therefore might have developed IDA at a higher extent because of a longer period of ID related to an inadequate iron intake and losses by menses as discussed above for nonathletes. Thus, the low number of years menstruating may possibly explain the nonsignificant difference compared with nonathletes.

It is known that serum iron decreases during active training, and this is probably due to the inflammatory response of physical activity.\(^{12}\) Physical exercise starts an acute-phase response leading to postexercise levels of cytokines comparable with those seen in severe burns, inflammatory disease, or bacterial infections.\(^{23,24}\) Intense physical training can induce a 2- to 3-fold increase in pro-inflammatory cytokine levels of tumor necrosis factor-\(\alpha\) and interleukin (IL)-1\(\beta\),\(^{25}\) and also the cytokine IL-6.\(^{26}\) The increase in

<table>
<thead>
<tr>
<th>Lifestyle Factor</th>
<th>Athletes (n = 57)</th>
<th>Nonathletes (n = 92)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breakfast, No.</td>
<td>46</td>
<td>48</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Meals per day,</td>
<td>3.4 ± 0.6</td>
<td>3.0 ± 0.8</td>
<td>0.003*</td>
</tr>
<tr>
<td>Milk, No.</td>
<td>43</td>
<td>48</td>
<td>0.007*</td>
</tr>
<tr>
<td>Coffee, No.</td>
<td>7</td>
<td>20</td>
<td>0.21</td>
</tr>
<tr>
<td>Tea, No.</td>
<td>13</td>
<td>30</td>
<td>0.27</td>
</tr>
<tr>
<td>Dietary supplements, No.</td>
<td>17</td>
<td>14</td>
<td>0.056</td>
</tr>
<tr>
<td>Active weight loss, No.</td>
<td>24</td>
<td>58</td>
<td>0.020*</td>
</tr>
<tr>
<td>Hormonal contraception, No.</td>
<td>17</td>
<td>44</td>
<td>0.044*</td>
</tr>
<tr>
<td>Smokers, No.</td>
<td>5</td>
<td>25</td>
<td>0.009*</td>
</tr>
</tbody>
</table>

*Statistically significant (P < 0.05).
inflammatory cytokines, especially IL-6, stimulates the synthesis of hepcidin, a key regulator of iron metabolism, leading to lower levels of iron and transferrin.

In our study, ID could explain the anemia of all subjects in both groups and no case of anemia seems to be explained by sports anemia. The proposed mechanisms for sports anemia have included increased iron demand or increased losses through sweating, through intravascular mechanical hemolysis, or through the gastrointestinal tract. In recent years, dilution pseudoanemia has been widely accepted as the explanation, meaning that sports anemia today is not considered to be a true anemia by most researchers.

Thus, the most common cause for ID among females is the imbalance between dietary intake and losses. Therefore, we wanted to investigate the role of a number of lifestyle factors, such as intake of milk, the number of meals, breakfast, menses, active weight loss, intake of nutritional supplements, and a number of other factors, which could influence the iron balance (Table 3). Interestingly, the female athletes in the present study seem to have better eating habits that are shown by a greater number of meals including breakfast. This is important because in 2003 it was shown that those adolescents (females and males) who had the highest iron intake were those who ate 2 cooked meals per day. Among those who did not eat breakfast, 25% had a low intake of iron in that study. We also found that in the control group there was a statistically significant correlation between serum ferritin level and the number of meals.

The athletes did not differ in the time of menarche but reported lesser menstrual volume, which should mean less losses of iron. In an earlier study of elite women athletes, between 19 and 28 years of age (mean, 23.5 years), we found almost the same proportion of ID (57%) but a higher prevalence of IDA (29%) than in the present group (9%). The explanation of this finding can be that about one half of the female participants had a balance between iron intake and losses and the other half had an imbalance, through larger losses by menses but a similar intake of iron, explaining a greater occurrence of IDA with increasing age.

It is possible that female athletes, despite the presence of nutritional and menstrual factors that should favor a better iron status, still seem to be as iron deficient as the control group determined by the levels of serum iron, TIBC, and ferritin. However, being influenced by the effect of physical exercise on IL-6 and hepcidin iron status determined through the serum factors could give a false low iron status. According to our data, it is possible that the combination of a higher iron intake and lower losses by menses helps to keep up the iron stores in young female athletes to the level of nonathletes, since they do not have a higher frequency of IDA.

The main finding of this study is that ID and IDA are common among female adolescents, and as common among athletes as in nonathletes. These results are shown despite the findings of factors that should favor a better iron status in the athlete group, such as a higher iron intake and less menstrual bleedings. It is interesting to find that these conditions, which are well known, well defined, easy to diagnose, and easy to treat still, are so common worldwide among women.

Consequently, we recommend that female athletes should be assessed at regular intervals for hemoglobin level and iron status. Whether nonanemic subjects with lowered iron status should be treated is not clear at the moment. A trial of iron supplementation for at least 3 months might be advisable, given that some subjects could suffer from relative anemia.

REFERENCES

24. Margeli A, Skenderi K, Tzironi M, et al. Dramatic elevations of interleukin-6 and acute-phase reactants in athletes participating in the ultradistance foot race spartathlon: severe systemic inflammation and


