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FERRITIN LEVEL ANALYSIS TO IDENTIFY IRON DEFICIENCY IN QUALIFIED ATHLETES

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Abstract The world of elite sports is marked by intense physical and psychological strains, significantly augmenting the demands on athletes' bodies and rendering them susceptible to iron deficiency, and anemia, especially women athletes. Iron deficiency can have severe consequences, including heightened injury risks, delayed recovery following physical exertion, compromised immunity and diminished athletic performance. Notably, iron deficiency in athletes can persist without manifesting as anemia. Consequently, comprehensive research is crucial to identify iron deficiency states in athletes. Our study focused on researching the ferritin content and other indicators of iron metabolism in the blood of 159 qualified athletes (98 men and 61 women) who specialized in various sports. The research entailed the assessment of ferritin concentration, hemoglobin, iron content, red blood cell count, and hematocrit level. The findings revealed a considerable prevalence of hidden iron deficiency among female athletes, with 54% exhibiting prelatent iron deficiency and 16% presenting with latent iron deficiency. They require appropriate recommendations for treatment and prevention. The results of our research confirm the presence of the iron deficiency problem in athletes, especially women. Due to the above, identifying not only iron-deficiency anemia but also hidden iron deficiencies is crucial to ensure timely and effective treatment and prevention.

Key words: iron deficiency anemia, sport, female athletes, sex differences

Introduction

Approximately 1,2 billion people worldwide suffer from iron deficiency anemia and iron deficiency without anemia (Kassebaum et al., 2014). It is necessary to notice that the above concepts are considered synonymous, but this is a false opinion. Iron deficiency without anemia is a broader concept and indicates low iron reserves in the body, regardless of anemia (Al-Naseem et al., 2021). Symptoms of iron deficiency can be nonspecific and manifest themselves in the form of fatigue, difficulty concentrating, sleep problems, and a decrease in physical capabilities, which significantly impact a person's health and performance (DiSilvestro et al., 2020, Coates et al., 2017, Sim et al., 2019).

The problem of iron deficiency also applies to athletes. The main causes of iron deficiency in athletes include (Damian et al., 2021):

1. Iron loss due to excessive sweating, hematuria, gastrointestinal bleeding, nutritional changes (unbalanced nutrition, vegetarianism, consumption of foods that reduce iron absorption), and during menstruation.
2. Diseases of the gastrointestinal tract caused by loads (malabsorption syndrome).
3. Inflammation and intravascular/extravascular hemolysis that occur in response to significant physical exertion.

In assessing iron deficiency and in order to gain a better understanding of the physiological processes occurring in the body, scientists propose to be guided by the following classification of the stages of iron deficiency states (Damian et al., 2021, Alaunyte et al., 2015):

1. The prelatent stage of iron deficiency is characterized by decreasing tissue iron stores, increased iron resorption in the small intestine (according to radiological studies) and the presence of sideroblasts in the bone marrow. Hemoglobin and iron transport fund preserved. Peripheral blood counts and serum iron levels are within the normal range. There are no clinical manifestations.
2. The latent stage is characterized by the depletion of not only tissue reserves of iron but also a decrease in the level of its transport form, and the disappearance of sideroblasts in the bone marrow. Characteristic is the preservation of hemoglobin fund (no anemia). Peripheral blood values are normal or slightly changed.

   There is a decrease in serum iron levels, and an increase in the total iron-binding capacity of serum, while red blood cells can be microcytic and hypochromic. The clinical picture is due to trophic disorders and manifestations of sideropenic syndrome.
3. Iron deficiency anemia is characterized by a more pronounced depletion of tissue reserves of iron and mechanisms to compensate for its deficiency, deviation from the norm of blood parameters, and clinical manifestations of sideropenic, general anemic, visceral syndromes and secondary immunodeficiency syndrome.

According to Sim et al. (2019), iron deficiency is observed in about 15–35% of female and 5–11% of male athletes. Other sources point to an even higher percentage of athletes with iron deficiency (up to 50% in women and up to 30% in men) (Koehler et al., 2011, Tan et al., 2012).

The most specific laboratory marker of iron deficiency is the serum ferritin content in the blood (Clénin et al., 2015). In their work, Nabhan et al. (2020) recommend using criteria based on threshold values of serum ferritin for detecting iron deficiency in athletes. The following distribution of ferritin threshold values in the blood allows us to divide athletes by their content into four groups:

1. feritin < 12 μg· l^{-1}. It is characterized by the depletion of iron stores in the bone marrow. It is used as the lower limit by laboratories, defining iron–deficiency anemia (the third stage of iron depletion).
2. < 20 μg· l^{-1} indicates latent iron deficiency (the second stage of iron depletion).
3. < 35 μg· l^{-1} indicates prelatent iron deficiency (the first stage of iron depletion).
4. < 50 μg· l^{-1} corresponds to the normal recommended threshold for men. Also, this threshold is recommended as a minimum level for training athletes for high-altitude training.

In turn, when assessing the presence of iron deficiency in athletes, it is important to note that Cook et al. (1992) note that the boundary optimal level of serum ferritin is not less than 45 μg· l^{-1}. Similar recommendations apply to athletes of both male and female sex (over 15 years old). In many scientific publications, ferritin values below 35 μg· l^{-1} are the minimum threshold for detecting iron deficiency in athletes and a recommendation for treatment with iron medications (Govus et al., 2015, Custer et al., 1995, WHO, 2020).

Summing up all the above, the minimum content of ferritin in the blood is 35 μg· l^{-1}, below which the appointment of iron medications for correction of iron deficiency and 45–50 μg· l^{-1} is recommended, as a minimum optimal level for athletes.

Because in sports of the highest achievements, the requirements for the athlete's body are especially high, the presence of iron deficiency becomes an even greater problem. It can have serious consequences, including an increased risk of injury, a slowdown in the recovery processes after physical exertion, a decrease in immunity, and a significant decrease in the performance and effectiveness of the athlete (Sim et al., 2019). It is equally important to consider that in many cases, iron deficiency in athletes can exist without the manifestation of anemia and have a latent flow. These highlight the necessity for conducting detailed studies on ferritin content for diagnosing iron deficiency states in highly trained athletes.

The purpose of the study

Research the content of ferritin and other indicators of iron metabolism in the blood of qualified athletes specializing in various sports in order to identify iron deficiency conditions.

Material and methods

Subjects

The study, which was conducted on the basis of the State Scientific Research Institute of Physical Culture and Sports (Kyiv, Ukraine), involved 159 qualified athletes, including 98 men and 61 women (Table 1). The average age of athletes – men 23,67 ± 4,10 years, women 22,59 ± 6,37 years.

Table 1. Number of athletes participating in the study by sport (n = 159)

Sport	Men (n = 98)	Women (n = 61)
Track and field athletics	23	44
Freestyle wrestling	8	7
Modern pentathlon	15	–
Beach volleyball	4	2
Canoeing	8	–
Rowing	3	–
Boxing	25	8
Greco-Roman wrestling	12	–

The anthropometric characteristics of athletes are presented in Table 2 (Table 2).

Table 2. Athletes' anthropometric indicators ($\bar{x}$ ± σ; n = 159)

Indicators	Men (n = 98)	Women (n = 61)
Height, cm	180,91 ± 9,72	171,63 ± 8,40
Body weight, kg	106,28 ± 4,65	76,09 ± 17,11
Body fat, %	25,04 ± 3,64	20,53 ± 6,61
Fat-free mass, kg	85,92 ± 20,96	59,63 ± 9,35

Ethics

The research was conducted following the basic bioethical norms of the Declaration of Helsinki of the World Medical Association on Ethical Principles of Scientific and Medical Research, as amended (2000, as amended in 2008), the Universal Declaration on Bioethics and Human Rights (1997), and the Council of Europe Convention on Human Rights and Biomedicine (1997). Each study participant provided written informed consent to participate in the study.

Laboratory research

The concentration of hemoglobin, the number of red blood cells, and the level of hematocrit were determined in the peripheral blood of athletes on the hematological analyzer «Erma–210» (Japan). Ferritin concentration and iron content were determined in serum using a ChemWell enzyme-linked immunosorbent analyzer (Awareness Technology, USA) using AccuBind ELISA test systems (Monobind Inc., USA) and reagent kits from Pointe Scientific Inc (USA).

Blood was taken in the morning on an empty stomach. Blood samples were taken from the ulnar vein. Their subsequent processing was carried out in accordance with the manufacturer's instructions.

Statistical analysis

All statistical analyses were performed using «Microsoft Excel 2016». The following statistical parameters were determined: mean ($\bar{x}$), standard deviation (σ), and interquartile range (IQR) to determine the distribution of ferritin in the blood of athletes in order to compare the results with studies by other authors.

Results

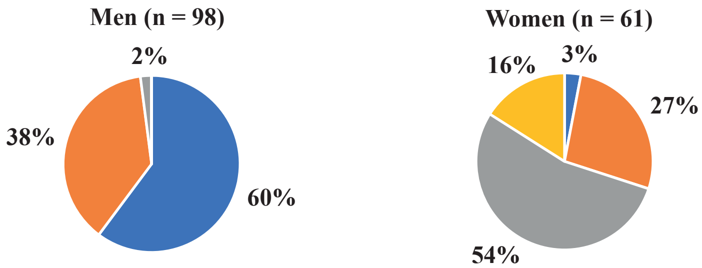
The World Health Organization (WHO) defines the diagnosis of iron-deficiency anemia based on the threshold values of hemoglobin content in the blood. For men, these levels are at least 130 g· l^{-1}, and for nonpregnant women – at least 120 g· l^{-1} (WHO, 2020, Hasan et al., 2022). As can be seen from the data presented in Table 3, the average hemoglobin content in both men and women is above the lower limit of the norm, indicating the absence of iron deficiency anemia in athletes of both sexes (Table 3). The number of red blood cells and the level of hematocrit are also within the normal range, which is 4,0–5,5· 10^{-12}/l for male athletes; for women – 3,7–4,7 10^{-12}/l (red blood cells) and a hematocrit content of 40–52% for men; for women 37–47%.

We found that the average concentration of ferritin in serum in men is 88,86 μg· l^{-1} (interquartile range 34–130 μg· l^{-1}), which is the norm for men. However, in women, the average ferritin content is an average of 27,83 μg· l^{-1} (interquartile range 11,23–44,4 μg· l^{-1}), which is classified by Nabhan et al. (2020) the stage of prelatent iron deficiency (first stage of iron depletion). In addition, this value of the average ferritin content is one of the signs of prelatent iron deficiency according to the classification proposed by Peeling et al. (2007), in which there is hemoglobin content > 115 g· l^{-1}, and ferritin content > 35 µg· l^{-1}.

Table 3. Athletes` blood indicators ($\bar{x}$ ± σ; n = 159)

Indicators	Men (n = 98)	Women (n = 61)
Hemoglobin, g· l^{-1}	152,82 ± 8,74	132,41 ± 6,73
Red blood cells,· 10^{-12}/l	5,34 ± 0,27	4,64 ± 0,22
Hematocrit, %	47,34 ± 3,25	41,74 ± 2,01
Iron, µmol· l^{-1}	30,38 ± 13.56	22,61 ± 6,75

For a more detailed analysis of the ferritin content in the athletes' blood, we divided them into groups according to the classification Nabhan et al. (2020), based on the distribution of blood ferritin threshold values (Figure 1).



Note. Ferritin content, µg· l^{-1} (> 50 35–50 20–35 < 20)

Figure 1. Distribution of athletes (percentage) by blood ferritin content (n = 159)

As can be seen from the data in Figure 1, a significant number of male athletes (60% of 98 athletes) have a ferritin content of more than 50 µg· l^{-1}, and 38% – from 35 to 50 µg· l^{-1}. Such ferritin levels are considered normal values for the general population. Only 2% of male athletes have a ferritin content below 35 µg· l^{-1}.

Among women, the highest percentage (54% of 61 athletes) are those with a ferritin content of 20 to 35 µg· l^{-1}. In turn, 16% (10 athletes) have a ferritin content of less than 20 µg· l^{-1}. These data suggest that most female athletes (70%) have a prelatent or latent iron deficiency.

Serum iron content in both men and women is within the normal range (Table 3). Normally, the iron content in blood serum is 11,6–30,4 µmol· l^{-1} for men and women 8,9–30,4 µmol· l^{-1}, respectively.

Discussion

Our study aimed to determine the content of ferritin and some other indicators of iron metabolism in the blood of qualified athletes specializing in various sports in order to identify iron deficiency conditions. The absence of iron deficiency in the athlete's body is important because iron deficiency can have significant consequences for the athlete, which will lead to a decrease in performance and effectiveness (Sim et al., 2019). It was found that as a result of a lack of iron reserves, the body's ability to transfer oxygen to working muscles decreases. A close relationship between iron content, hemoglobin concentration, maximum oxygen consumption, and aerobic exercise performance was also found (Nabhan et al., 2020, Chatard, 1999). It is important to note that iron deficiency even without anemia reduces the effectiveness of exercise (DellaValle & Haas, 2011, DellaValle & Haas, 2012).

As a result of our study, athletes of both sexes have no signs of iron deficiency anemia. Almost all male athletes' ferritin values are within the normal range, indicating the absence of iron deficiency. Meanwhile, the majority of women have either prelatent or latent iron deficiency (70% out of 61 female athletes). The results of our study are consistent with the results of a study carried out by Jack et al. (2023), in which it was found that approximately 68% of ballet dancers suffered from iron deficiency. In addition, the work of Disilvestro et al. (2020) revealed an even greater percentage of women actively engaged in healthy running, who have an iron deficiency. Almost all female athletes, with the exception of 2 of 39, had a ferritin content below 35 µg· l^{-1}, which was proposed, according to their classification, as stage 1 of iron deficiency in athletes (ferritin content was 15–35 µg· l^{-1}). The results of our research and other authors (Disilvestro et al., 2020, Jack et al., 2023, Husarova & Vdovenko, 2023) indicate the presence of a serious problem of iron deficiency conditions among female athletes and require appropriate recommendations for the treatment and prevention of iron deficiency conditions.

In order to compare the results of our studies with the works of other authors, we used data from Nabhan et al. (2020), which are based on the distribution of athletes by blood ferritin content. The above authors in their work determined that in male athletes the average ferritin content was 74,0 µg· l^{-1} (interquartile range 45,5–112,0 µg· l^{-1}), in female athletes 33,0 µg· l^{-1} (interquartile range 30,7–51,3 µg· l^{-1}). In turn, the following average values were characteristic for the general population according to Custer et al. (1995): for men aged 20–24 years – 90,2 µg· l^{-1} (interquartile range 58,6–131,0 µg· l^{-1}); age 24–28 years – 105 µg· l^{-1} (76,9–172 µg· l^{-1}). For women (20–24 years) – 31,8 µg· l^{-1} (interquartile range 18,6–52,3 µg· l^{-1}) and aged 24–28 years – 38,8 µg· l^{-1} (22,5–63,4 µg· l^{-1}).

As a result of our study, in which we divided athletes into groups depending on sex and according to the threshold values of ferritin content (12, 20, 35 and 50 µg· l^{-1}), it was found that the average concentration of ferritin in the blood of male athletes is 88,86 µg· l^{-1} (interquartile range 34–130 µg· l^{-1}), in women – 27,83 µg· l^{-1} (interquartile range 11,23–44,4 µg· l^{-1}). The data we obtained on male athletes differ from the values of the general population of men and are slightly higher than the data of athletes obtained by Nabhan et al. (2020). In turn, the average value of ferritin in female athletes is lower and differs both from the data of the general population of women and from the data of the results of studies conducted among athletes, which were described above.

Following a detailed analysis of the ferritin content distribution, it was found that only 2% of male athletes had ferritin values less than 35 µg·l^{-1}, and there were no athletes with ferritin values less than 20 µg·l^{-1}. In turn, the studies of Nabhan et al. (2020) observed a decrease in ferritin content of less than 35 µg· l^{-1} in 15% of athletes and below 20 µg· l^{-1} – 3%. That is, the data we obtained indicate a smaller percentage of athletes (only 2%) who require correction of iron deficiency.

In our studies, 16% of female athletes were found to have ferritin values less than 20 µg·l^{-1} and 54% had values less than 35 µg·l^{-1}. Consequently, 70% of female athletes have a prelatent or latent iron deficiency. According to the above authors, female athletes also had a significant prevalence of iron deficiency (in 23% of qualified athletes, the ferritin content was lower than 20 µg· l^{-1} and 52% – less than 35 µg· l^{-1}). The data of our study coincide with the percentage of women with a ferritin content of less than 35 µg· l^{-1}, but we found a slightly lower percentage of women with a ferritin content of > 20 µg· l^{-1} compared to the data of Nabhan et al. (2020). Discrepancies can be due to many factors, such as the various sports that were included in the study, the geographical features of the conduct (country), climatic conditions, nutritional characteristics, the presence of medical aspects, etc.

Despite the differences in the average values of ferritin content compared to the results of previous studies in sports (Disilvestro et al., 2020, Nabhan et al., 2020, Custer et al., 1995), the data obtained by us fully confirm the fact of the problem of iron deficiency in athletes and the need for routine screening to detect not only iron deficiency anemia, but also a hidden iron deficiency in the body (prelatent and latent stages of iron deficiency).

Athletes are recommended to undergo screening for the detection of iron-deficiency states and prevention of anemia twice a year (Clénin et al., 2015). Researchers agree, despite many blood parameters, that for the routine clinical evaluation of iron deficiency anemia in sports, it is enough to determine the following indicators: hemoglobin concentration, ferritin, and transferrin saturation (Clénin et al., 2015, Peeling et al., 2007).

It is extremely important to note that the minimum threshold for ferritin content in the blood of athletes is recommended values not lower than 45–50 μg· l^{-1} (Cook et al., 1992). Athletes with lower serum ferritin levels need to pay special attention to maintaining an optimal level of iron in the body (Govus et al., 2015, Nielsen & Nachtigal, 1998, Solberg & Reikvam, 2023). This is possible by identifying and eliminating the causes leading to its deficiency and/or adjusting the diet. After eliminating the factors that cause iron deficiency, recovery of optimal iron levels can be achieved through a balanced diet, which includes increased consumption of foods high in iron (Vdovenko et al., 2015).

Practical recommendations for correcting the diet of athletes:

1. Increase the content of products with high iron content. The main sources of iron are precisely products of animal origin (liver pork, chicken, veal, meat, poultry, kidneys, etc.);
2. Foods with high levels of phytin, such as cereals and flour products, are recommended to be combined with products rich in vitamin C (berries, citrus fruits, kiwi, etc.);
3. Exclude from the diet foods rich in phytates (instant oatmeal, nuts, seeds, whole grain bread, etc.);
4. Remove from the diet tea and coffee;
5. Do not eat at the same time foods containing iron and foods high in calcium, copper, and magnesium.

If athletes have iron deficiency, a doctor's consultation is mandatory regarding additional iron supplementation. According to the recommendation of the British Society of Gastroenterology (Snook et al., 2021), traditional oral iron salts (ferrous sulfate, ferrous gluconate, and ferrous fumarate) are inexpensive, effective, safe, and readily available—and they remain the standard therapies for iron deficiency anemia. The recommended standard daily therapeutic dose of elemental iron is 100–200 mg. Traditionally oral iron salts were taken as a split dose, two or three times a day (Snook et al., 2021, Liberal et al., 2020).

Conclusions

1. As a result of the study iron deficiency anemia was not detected in subjects of both genders. Nevertheless, a significant number of female athletes (70%) have a hidden (prelatent and latent stages) iron deficiency.
2. It was found that 54% of women and 2% of men have prelatent iron deficiency. In turn, 16% of athletes have latent iron deficiency, which requires appropriate recommendations for treatment and prevention.
3. The results of our studies confirm the presence of the problem of iron deficiency in athletes and indicate the importance of identifying not only iron deficiency anemia but also hidden iron deficiency in order to timely ensure effective treatment and prevention.

Prospects for further research

The presence of iron deficiency in athletes requires further detailed scientific research in representatives of various sports, taking into account a variety of possible factors in order to increase the effectiveness of training and competitive activity of athletes.

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