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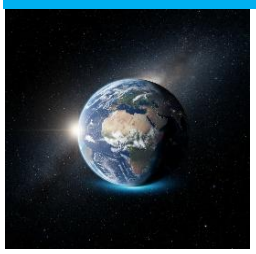

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Iron Deficiency and Beyond: Implications for Cognitive Function and Recovery in Female Endurance Athletes

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Abstract

Purpose

This narrative review evaluates the systemic impact of iron deficiency (ID) in female endurance athletes, focusing on cognitive function, mitochondrial bioenergetics, and tissue recovery processes beyond traditional erythropoiesis.

Materials and methods

A comprehensive literature search was conducted across PubMed, Scopus, and Google Scholar databases, covering peer-reviewed publications from 2003 to 2025. A total of 31 key sources were analyzed, focusing on non-anemic iron deficiency (IDNA) and the regulatory role of hepcidin.

Results

Evidence demonstrates that iron is a critical cofactor for neurotransmitter synthesis (dopamine, serotonin) and the mitochondrial electron transport chain. Subclinical iron depletion impairs executive planning, attentional focus, and metabolic efficiency, often manifesting as "brain fog" and prolonged recovery times. Furthermore, exercise-induced interleukin-6 (IL-6) triggers a hepcidin surge 3–6 hours post-training, which degrades ferroportin channels and reduces fractional iron absorption by approximately 36%.

Conclusions

Effective iron management requires a "timing-first" approach, including monitoring serum ferritin (target 30–50 ng/mL) and utilizing alternate-day oral dosing (60–200 mg) in a fasted, early-morning state. Transitioning from reactive anemia treatment to proactive iron optimization, incorporating cognitive health markers into routine screening, is essential to safeguard the performance potential and long-term well-being of female endurance athletes.

Key words: female endurance athletes, non-anemic iron deficiency (IDNA), cognitive function, recovery, iron supplementation strategies, hepcidin

List of Abbreviations:

ATP – Adenosine triphosphate
CNS – Central Nervous System
CRP – C-reactive protein
ETC – Electron transport chain
Fe-S – Iron-sulfur clusters
Hb – Hemoglobin
ID – Iron deficiency
IDA – Iron Deficiency Anemia
IDE – Iron-Deficient Erythropoiesis
IDNA – Iron Deficiency Non-Anemia
IL-6 – Interleukin-6
MeSH – Medical Subject Headings
REDs – Relative Energy Deficiency in Sport
RPE – Rating of Perceived Exertion
sTfR – Soluble transferrin receptor
T3 – Triiodothyronine
T4 – Thyroxine
TfS / TSAT – Transferrin saturation
TIBC – Total iron-binding capacity
TPO – Thyroid peroxidase
VO_2max – Maximal oxygen consumption

1. Introduction

Modern female endurance sport is undergoing a dynamic evolution, reflected in the record number of female athletes competing in marathons, triathlons, and ultra-endurance

events. This growing participation highlights the unique physiological demands of the female body, including specific requirements for essential micronutrients. Among these, iron plays a pivotal role; it is not merely a cornerstone of oxygen transport but, crucially, a fundamental cofactor in enzymatic processes that determine energy metabolism and the homeostasis of the central nervous system (1).

Iron deficiency (ID) remains the most prevalent nutritional deficit among athletes, affecting—according to various estimates—between 15 and 35% of active women (2). A particular diagnostic challenge, often termed the "paradigm of hidden deficiency," is Iron Deficiency Non-Anemia (IDNA). In this stage, hemoglobin levels remain within clinical norms, frequently leading to the misdiagnosis of iron adequacy. However, even in the absence of clinical anemia, depleted tissue iron stores significantly impair cellular enzymatic activities and oxygen homeostasis (3). Consequently, such subclinical deficits are insufficient to maintain optimal metabolic functions and can jeopardize the overall health and performance of the athlete.

The present paper extends beyond the traditional focus on iron in the context of physical performance (the "beyond the muscle" approach). Recent evidence suggests that subclinical iron deficiencies in female athletes may lead to significant cognitive impairments, including diminished concentration, mood disturbances, and prolonged reaction times. In endurance disciplines, these factors directly translate into impaired decision-making capabilities under conditions of progressive fatigue (4). Furthermore, iron is critical for tissue repair and recovery processes; inadequate supply may hinder training adaptation by negatively impacting mitochondrial biogenesis and endocrine balance (5).

The aim of this narrative review is to evaluate the existing literature on the effects of iron deficiency on cognitive function and recovery capacity in female endurance athletes. This review seeks to integrate biochemical mechanisms with applied sports practice and to propose evidence-based recommendations for optimal iron status monitoring and supplementation strategies in this specific athletic population.

2. Materials and methods

This narrative review explores the physiological and neurocognitive implications of iron deficiency, with particular focus on iron deficiency without anemia (IDNA) and the regulatory

role of hepcidin in female endurance athletes. These interrelated mechanisms are central to energy metabolism, cognitive functioning, and recovery processes, and their disruption may adversely influence athletic performance, mental capacity, and long-term health.

The literature search was conducted using PubMed, Scopus, and Google Scholar, supplemented by searches of Springer, Elsevier, and MDPI platforms. Only peer-reviewed original research articles and narrative or systematic reviews published in English were included.

“Female athletes”, “endurance sports”, “iron deficiency”, “non-anemic iron deficiency”, “hepcidin”, “cognitive function”, “recovery”, “iron supplementation”, and “ferritin” were the MeSH terms.

We included 33 articles published between 2003 and 2026. No formal time limits were imposed, although the search strategy prioritized recent high-quality studies while also incorporating key earlier publications to provide a comprehensive overview of the topic.

Only studies conducted in humans, focusing on female athletes or physically active women, published in English, and addressing iron metabolism and its functional effects were included. Studies involving only sedentary populations or animal models were excluded, except when used to clarify underlying mechanisms.

Initially, 51 articles were identified. After removing duplicates and excluding studies that focused on non-active populations, lacked relevance, or were not published in English, a total of 34 studies were included in the final analysis.

Identification

Records identified via PubMed, Scopus, and publishing platforms (Springer, Elsevier, MDPI) *(n = 51)*

Screening

Records included after title and abstract screening and application of exclusion criteria *(n = 34)*

Excluded

1 article (duplicate entry)

1 article (language barrier - non-English publication)

15 articles (sedentary populations, animal models, or unrelated nutrients) *(n = 17)*

Eligibility

Full-text articles assessed for eligibility

(n = 34)

Included

Final studies analyzed

(n = 34)

The studies were selected through a systematic, multi-step procedure in accordance with a structured framework based on PRISMA methodology.

3. Pathophysiology of Iron Deficiency in Female Athletes

3.1. Exercise-Induced Mechanisms of Iron Loss

In female endurance athletes, iron deficiency is rarely the result of a single factor; rather, it arises from a synergy of physiological and exercise-induced mechanisms (2, 6). Beyond the basal iron loss associated with the menstrual cycle, several sport-specific pathways contribute to a negative iron balance, with menstrual blood loss acting as an important initial trigger for adaptations in iron metabolism (7). Foot-strike hemolysis, caused by repeated mechanical impact during running, leads to the destruction of erythrocytes in the capillaries of the feet, subsequently increasing iron turnover (8, 9). Furthermore, intense endurance exercise can cause transient splanchnic hypoperfusion, resulting in gastrointestinal microbleeding and compromised gut integrity (10). Additional, though smaller, amounts of iron are lost through dermal excretion (sweat) and exercise-induced hematuria, which can become significant in athletes with high training volumes (11).

3.2. The Role of Hepcidin in Iron Regulation

A central element in the pathophysiology of iron deficiency in athletes is hepcidin, a liver-derived peptide hormone that acts as the primary gatekeeper of systemic iron homeostasis. The regulation of iron via hepcidin is particularly sensitive to the physiological stress induced by endurance training.

Endurance exercise triggers an acute inflammatory response, characterized by a significant transient increase in circulating interleukin-6 (IL-6). This rise in IL-6 stimulates the hepatic production of hepcidin, which typically peaks approximately 3 to 6 hours post-exercise (2). Hepcidin regulates systemic iron homeostasis by binding to and inducing the degradation of ferroportin, the sole known cellular iron exporter expressed on enterocytes and macrophages, thereby acutely reducing both intestinal iron absorption and iron recycling from macrophage stores. Endurance exercise induces a transient post-exercise increase in circulating hepcidin concentrations, creating a temporal "hepcidin window" during which iron availability is reduced. This exercise-induced hepcidin response has been identified as an important regulatory mechanism that may contribute to the development of iron deficiency in female endurance athletes, even in the presence of adequate dietary iron intake (2 ,12).

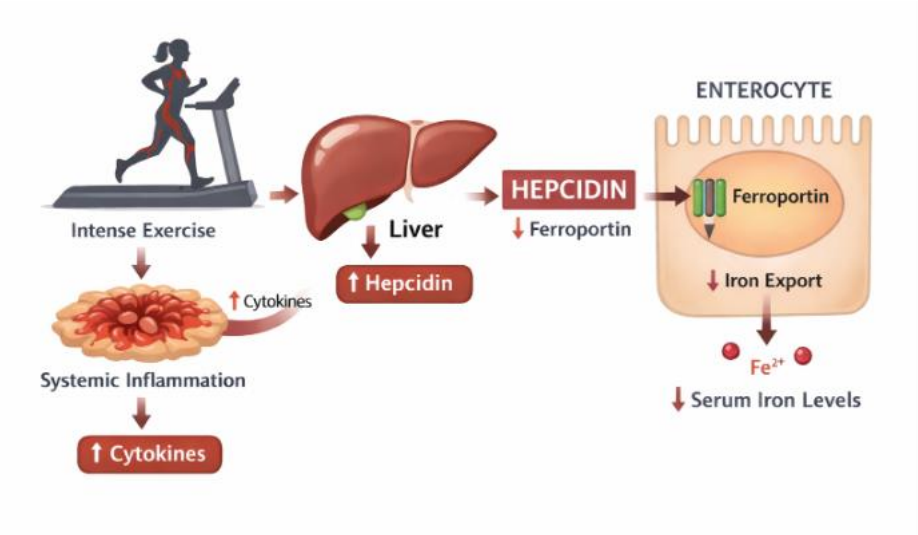

Figure 1. Post-exercise inflammation–hepcidin–ferroportin axis showing IL-6–induced hepcidin increase and subsequent ferroportin degradation, reducing iron export from enterocytes.

3.3 Stages of Iron Depletion: From Sequestration to Anemia

A comprehensive understanding of the systemic consequences of iron deficiency requires a clear differentiation between its progressive stages. This staged framework is particularly relevant in female endurance athletes, as impairments in cognitive function,

recovery capacity, and overall physiological efficiency may emerge well before iron deficiency progresses to clinically overt anemia (3).

Stage I (Iron Depletion) is defined by a reduction in body iron stores, most commonly reflected by decreased serum ferritin concentrations, while hemoglobin levels remain within the normal reference range. At this stage, oxygen transport capacity is preserved; however, the depletion of tissue iron initiates early disruptions in iron homeostasis. As iron availability becomes limited, physiological prioritization favors erythropoiesis over non-hematological processes, which can already compromise metabolic efficiency and neuromuscular function. Due to the absence of anemia and subtle clinical presentation, this stage frequently remains undetected in routine sports medical screening (1, 12).

Stage II (Iron-Deficient Erythropoiesis) occurs when iron availability becomes insufficient to fully support erythropoiesis and the synthesis of iron-dependent enzymes and non-heme proteins, including mitochondrial cytochromes involved in oxidative metabolism. Although hemoglobin concentrations may still fall within clinical reference limits, biomarkers such as serum iron and transferrin saturation are typically reduced. During this stage, athletes may experience symptoms extending beyond impaired physical performance, including reduced concentration, mood disturbances, and delayed recovery, highlighting iron's critical role in neurological and cellular processes independent of oxygen transport (5,13).

Stage III (Iron Deficiency Anemia; IDA) represents the final and most severe stage, characterized by a decline in hemoglobin concentrations below established diagnostic thresholds (typically <12 g/dL in women). This results in a pronounced reduction in oxygen-carrying capacity, leading to diminished aerobic performance (VO_2max), chronic fatigue, and exertional dyspnea. At this stage, the functional consequences of iron deficiency become overt and substantially impair both athletic performance and general health (5, 14).

Stage	**Characteristics**	**Biomarkers**	**Functional Consequences**	**Clinical Notes**

I – Iron Depletion	Decreased iron stores; hemoglobin levels remain unaffected	↓ Ferritin, normal Hb, TSAT and serum iron	Early metabolic and neuromuscular disruptions; possible fatigue and reduced concentration	Often undetected in routine screening; pre-anemic stage
II – Iron Deficient Erythropoiesis (IDE)	Iron deficiency limits support for erythropoiesis and non-heme enzymes	↓ TSAT, ↓ serum iron, ↑ TIBC, Hb still within normal range	Impaired concentration, mood disturbances, delayed recovery, reduced aerobic capacity	Subclinical stage; symptoms may appear despite normal Hb
III – Iron Deficiency Anemia (IDA)	Hemoglobin below normal (<12 g/dL in women)	↓ Hb, ↓ ferritin, ↓ serum iron and TSAT, ↑ TIBC	Significant reduction in oxygen transport; reduced (VO_2max), chronic fatigue, exertional dyspnea	Clinically overt anemia; marked impact on physical performance and health

Table 1. Stages of iron deficiency in female endurance athletes, from iron depletion to iron deficiency anemia, showing biomarkers and functional consequences (14, 28).

4. The Impact of Iron Deficiency on Cognitive Function in Female Athletes

4.1. Neurotransmission and Brain Homeostasis

Iron is an essential cofactor for tyrosine hydroxylase, the rate-limiting enzyme in dopamine synthesis, and plays a pivotal role in the production of other monoamine neurotransmitters, including serotonin and norepinephrine (15, 16). Dopamine is critical for motivation, executive function, and reward processing, all of which are essential for sustaining effort during prolonged physical exertion, including endurance exercise (17). Consequently, iron deficiency may impair dopaminergic neurotransmission and negatively affect cognitive performance, reducing mental drive and resilience during high-intensity training or competition.

Experimental studies in animal models have demonstrated that iron deficiency can reduce dopamine transporter function and D2 receptor density, providing mechanistic insight into how iron may affect motivation and reward signaling (15). Even without anemia, subclinical iron deficiency (IDNA) has been linked to lower iron levels in certain brain regions. While this has been observed in adolescent females, it suggests that similar mechanisms could also affect other groups at risk for iron deficiency, including female endurance athletes, potentially impacting cognitive functions such as attention, executive function, and mental drive (17, 18).

Beyond dopamine, iron is required for oligodendrocyte function and myelin maintenance, which are crucial for neuronal signal conduction and neuroplasticity. Deficient brain iron stores may therefore impair motor learning, strategy adjustment, and cognitive flexibility—abilities essential for optimal performance in endurance disciplines (16, 17). In a comprehensive review, Gao et al. (2025) further corroborate these findings, underscoring that iron is a fundamental requirement for maintaining neural integrity and metabolic homeostasis throughout the lifespan. Their analysis highlights that even marginal iron deficiencies can disrupt the complex neural networks responsible for neurotransmitter regulation and brain health (17).

4.2. Cognitive Processing, Reaction Time, and Perceived Exertion

In endurance sports such as marathons or triathlons, the ability of the Central Nervous System (CNS) to process information efficiently under conditions of progressive fatigue is a key determinant of performance. Athletes with depleted iron stores often exhibit significant impairments in attentional focus and information processing speed. Specifically, research indicates that body iron status is significantly associated with executive planning functions,

which are essential for maintaining complex pace strategies and tactical decision-making during competition (11, 19).

Recent clinical observations in physically active women indicate that iron deficiency, even in the absence of anemia, is frequently associated with subjective cognitive symptoms, including reduced concentration, mental fatigue, and impaired clarity of thought, which may negatively affect both training quality and post-exercise recovery (20). Such alterations in cognitive functioning are particularly relevant in endurance disciplines that require sustained attention, rapid information processing, and precise motor control, where lapses in focus may increase the risk of technical errors or injury.

Emerging evidence further suggests that iron deficiency contributes to central fatigue by influencing the brain's perception of effort. Women with suboptimal iron status report higher levels of perceived exertion during exercise performed at comparable physiological workloads, indicating an altered psychophysical response to endurance stress (20). This elevated Rating of Perceived Exertion (RPE) may reflect increased neural effort required to maintain performance under conditions of impaired iron availability. Consequently, iron deficiency may lead to premature psychological exhaustion, limiting endurance capacity before the full aerobic potential is physiologically reached (20, 22).

5. Impact on Recovery and Tissue Repair

5.1. Mitochondrial Function and Energy Production

While the role of iron in oxygen transport via hemoglobin is well-established, its function within the cellular bioenergetic framework is equally critical for endurance performance. Iron is a fundamental component of the electron transport chain (ETC), serving as a key constituent of cytochromes and iron-sulfur (Fe-S) clusters. These proteins are essential for the transfer of electrons required to generate adenosine triphosphate (ATP) through oxidative phosphorylation (5).

Research indicates that mitochondrial iron deficiency can impair enzymatic activity long before a decline in hemoglobin levels is observed. Specifically, a reduction in the activity of iron-dependent enzymes, such as succinate dehydrogenase, limits the muscle's oxidative capacity (23). For female endurance athletes, this mitochondrial dysfunction results in a lower anaerobic threshold and an increased reliance on glycolytic pathways at submaximal intensities.

This metabolic shift leads to accelerated lactate accumulation and a significantly prolonged recovery period between high-intensity training sessions, as the resynthesis of ATP and the clearing of metabolic byproducts are compromised by inefficient mitochondrial respiration (5, 24). Furthermore, iron is essential for mitochondrial homeostasis; therefore, chronic deficiency may hinder the metabolic adaptations of skeletal muscle to aerobic training (23, 24).

5.2 Thyroid Hormone Metabolism and Thermogenesis

Iron plays a fundamental role in maintaining hormonal homeostasis, serving as an indispensable element for thyroid function. It is a critical cofactor for thyroid peroxidase (TPO)—a heme-dependent enzyme essential for the synthesis of thyroid hormones (14). Iron deficiency, even in its non-anemic stage (IDNA), can significantly disrupt the hypothalamic-pituitary-thyroid axis, leading to a reduction in the basal metabolic rate, which is particularly detrimental to female athletes during the recovery process (12, 18).

A key mechanism linking iron status to athletic performance is the conversion of thyroxine (T4) into its biologically active form, triiodothyronine (T3). The enzymes responsible for this transformation, deiodinases, are indirectly dependent on iron availability. Research suggests that iron deficiency limits this conversion, resulting in lower circulating levels of T3 (18). For endurance athletes, this may manifest not only as generalized lethargy but also as impaired thermogenesis. A reduced ability to maintain core body temperature and increased sensitivity to cold can negatively impact training comfort in variable weather conditions and slow down tissue repair processes that occur during sleep (17, 18).

Furthermore, chronic iron deficiency may exacerbate or mask the symptoms of Relative Energy Deficiency in Sport (REDs), where thyroid dysfunction is a recognized component of the female athlete triad (10, 12). Consequently, optimizing ferritin levels is essential not only for oxygen transport but also as a prerequisite for the metabolic and hormonal integrity required for high-level athletic competition (20).

5.3. Collagen Synthesis and Connective Tissue Integrity

The role of iron in an athlete's body extends beyond energy metabolism to include the structural regeneration of the musculoskeletal system. Iron is an essential cofactor for the enzymes prolyl hydroxylase and lysyl hydroxylase, which are responsible for modifying amino acids during collagen biosynthesis. This process is critical for the formation of stable cross-links within the collagen triple helix, providing tissues with the necessary mechanical strength and elasticity (14, 25).

Inadequate iron availability can lead to the weakening of the structure of tendons, ligaments, and articular cartilage. For female endurance athletes, who are subject to repetitive mechanical loading, impaired collagen synthesis translates into an increased risk of overuse injuries, such as tendinopathies or connective tissue micro-trauma (24, 25). Furthermore, iron supports the proliferation of fibroblasts, which is essential for rapid tissue healing and remodeling following strenuous exercise (17).

When combined with the hormonal disturbances described in section 4.2, iron deficiency creates an unfavorable environment for recovery, where tissue repair cannot keep pace with the micro-damage incurred during training. Optimizing iron status is therefore a fundamental element of injury prevention strategies and the long-term maintenance of musculoskeletal health in competitive female athletes (20, 25).

6. Practical Implications, Monitoring, and Supplementation Strategies

6.1. Monitoring Iron Status and Interpretation in Elite Athletes

Accurate assessment of iron status in female endurance athletes requires a sophisticated approach that moves beyond standard clinical reference ranges. Traditional laboratory norms for the general population often fail to account for the heightened physiological demands of high-volume training (3, 5). For competitive athletes, the primary focus should be on serum ferritin, transferrin saturation (TfS), and soluble transferrin receptor (sTfR) levels to distinguish between functional and absolute deficiency (2, 13). Furthermore, comprehensive monitoring of these biochemical profiles is essential for the early detection of subclinical deficiencies in endurance disciplines (32). Such diagnostic precision should be integrated into a broader framework of health-promoting behaviors, which significantly determine the overall quality of life and athletic longevity (33).

Current sports science consensus suggests that a serum ferritin level below 30 ng/mL should be classified as stage 1 iron deficiency (ID) in athletes, even if hemoglobin levels remain within normal limits (non-anemic iron deficiency) (13, 25). However, emerging evidence indicates that suboptimal iron stores may adversely affect cognitive function and executive processes in women, even in the absence of anemia (11, 19). When ferritin drops below 15–20 ng/mL, the risk of significant performance impairment and metabolic disruption increases dramatically (14, 24).

A critical challenge in monitoring is the fact that ferritin acts as an acute-phase reactant. Following intensive training or competition, systemic inflammation can artificially elevate ferritin levels via the IL-6 pathway, potentially masking an underlying deficiency (1, 2). To ensure diagnostic accuracy, blood samples should be collected in a rested state (at least 24 hours after strenuous exercise) and interpreted alongside C-reactive protein (CRP) (2, 23).

Furthermore, the interpretation of these biomarkers should consider the three-stage model of iron deficiency (22, 24). Stage 1 (Iron Depletion) is characterized solely by low ferritin; Stage 2 (Iron-Deficient Erythropoiesis) involves reduced TfS and elevated sTfR; and Stage 3 is reached when hemoglobin production is compromised, resulting in Iron Deficiency Anemia (IDA). Early detection during Stage 1 is crucial to prevent the "brain fog" and decreased mental drive often reported by athletes even before the onset of clinical anemia (20, 25).

6.2. Oral vs. Intravenous Supplementation Strategies

The selection of an appropriate iron supplementation protocol is a critical clinical decision that must consider the severity of the deficiency, the athlete’s gastrointestinal tolerance, and the strategic timing within the competitive season (1, 3). While the goal remains the restoration of iron stores to support both physiological and cognitive functions, the pathway to achieving this varies significantly in efficacy and athlete compliance.

Oral Supplementation remains the primary intervention for athletes in Stage 1 and Stage 2 iron deficiency (22). However, its effectiveness is often compromised by the regulatory hormone hepcidin. Research indicates that oral iron ingestion triggers a transient spike in serum hepcidin, which peaks approximately 6 hours post-ingestion and can remain elevated for up to 24 hours, subsequently inhibiting the absorption of any doses taken shortly thereafter (2). To overcome this "hepcidin block," modern sports nutrition guidelines recommend an alternate-

day dosing strategy (e.g., 60–200 mg of elemental iron every 48 hours). This protocol has been shown to maximize fractional iron absorption and significantly reduce gastrointestinal side effects such as nausea, abdominal pain, and constipation, which are the most common reasons for non-compliance among female athletes (26, 27).

Intravenous (IV) iron therapy is indicated in cases of severe iron deficiency (ferritin <20 ng/mL), documented intolerance or poor adherence to oral supplementation due to gastrointestinal adverse effects, and in situations requiring rapid repletion of iron stores prior to high-priority competitive events (2, 5, 14). IV administration enables direct systemic delivery, thereby bypassing intestinal absorption pathways and the regulatory constraints imposed by hepcidin (2). Consequently, this approach leads to prompt restoration of iron availability within both erythroid and non-erythroid compartments. Clinical observations in athletic populations further suggest that IV iron therapy may be associated with a rapid improvement in subjective cognitive symptoms, including enhanced mental clarity, reduced perceived fatigue, and improved overall psychophysical well-being (20, 21, 20).

To optimize the efficacy of oral iron supplementation protocols, strict management of dietary co-factors is required. Co-administration with vitamin C significantly enhances iron bioavailability, whereas concomitant intake of absorption inhibitors—including calcium-rich dairy products, coffee, and tea containing polyphenols and tannins—should be avoided for at least 2–3 hours following ingestion (15,16). Additionally, the utilization of newer iron formulations, such as iron bisglycinate or sucrosomial iron, may represent a valuable alternative strategy in athletes exhibiting heightened gastrointestinal sensitivity, improving both tolerability and long-term adherence (3,12).

6.3 Individualized Iron Supplementation Strategies and Practical Recommendations for Female Endurance Athletes

To achieve maximal efficacy, iron supplementation must be synchronized with the athlete's physiological "absorption window," which is primarily dictated by the post-exercise inflammatory response. Strenuous endurance training triggers an acute spike in interleukin-6 (IL-6), leading to an elevation of serum hepcidin that typically peaks 3–6 hours post-exercise and can remain elevated for up to 24 hours (2, 6, 27). During this period, iron absorption is severely impaired as hepcidin binds to and degrades the ferroportin channels necessary for iron

transport into the bloodstream (1, 17, 29). Clinical trials involving trained runners have demonstrated that this post-exercise hepcidin surge can reduce fractional iron absorption by approximately 36% compared to rest conditions (26).

Recent high-quality meta-analytical evidence confirms that while oral iron supplementation is highly effective in increasing serum ferritin and hemoglobin levels in athletes, the magnitude of these improvements is significantly influenced by the baseline iron status and the strategic timing of the intervention (30). Consequently, a personalized approach requires shifting iron intake to periods of basal hepcidin levels—typically early morning, in a fasted state, or before the first training session of the day (2, 6, 13). For athletes training at high altitudes, precise timing and the use of alternate-day dosing are essential to prevent the rapid depletion of iron stores while minimizing gastrointestinal distress (2, 31). Furthermore, the psychological dimension of athlete development, particularly self-regulation skills and effective stress management, plays a vital role in maintaining high performance levels and preventing burnout during demanding training periods (34). Integrating these psychological markers with precise biochemical monitoring of iron status provides a more comprehensive framework for safeguarding the well-being of female endurance athletes (33).

7. Discussion

The synthesis of current evidence demonstrates that iron deficiency (ID) in female endurance athletes is a multisystem disorder impacting oxygen transport, mitochondrial efficiency, and neurocognitive health. Even subclinical stages (IDNA), characterized by normal hemoglobin but depleted ferritin levels, significantly impair executive function and attentional capacity due to disrupted neurotransmitter synthesis and cerebral metabolic homeostasis. Consequently, maintaining serum ferritin above 30–50 ng/mL is essential to prevent "brain fog" and psychophysical fatigue, thresholds notably higher than standard clinical norms. Given that endurance disciplines require high levels of cognitive control, integrating subjective fatigue and recovery quality into monitoring frameworks is a crucial advancement in athlete management.

Furthermore, the post-exercise inflammatory response, specifically the spike in interleukin-6 (IL-6), triggers a hepatic release of hepcidin that peaks 3–6 hours after training. This surge degrades ferroportin channels, reducing fractional iron absorption by approximately 36% and rendering immediate post-training supplementation counterproductive. To optimize bioavailability, contemporary evidence strongly supports individualized, alternate-day dosing (every 48 hours) synchronized with basal hepcidin levels, typically in the early morning. While oral iron remains the primary intervention, its success depends on avoiding dietary inhibitors and accounting for stressors like altitude exposure. In cases of severe deficiency, intravenous therapy offers rapid restoration of stores, though its use must remain strictly evidence-based.

In conclusion, iron management in female athletes must transition from reactive treatment of anemia to proactive optimization of iron stores. By prioritizing a "timing-first" approach and incorporating cognitive health markers into routine screening, practitioners can effectively safeguard an athlete's performance potential and long-term well-being. Future research should utilize randomized controlled trials to further delineate the causal pathways between iron status and mental performance in elite populations.

Disclosure

Authors' Contributions:

Conceptualization, KB and WK; methodology, PT and PG; investigation, KB, NK, and SD; data curation, JF and NK; writing – original draft preparation, KB and PT; writing – review and editing, JF, WK, PG, and SD; supervision, NK. All authors have read and agreed to the published version of the manuscript.

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Conflict of Interest

The authors declare no conflicts of interest.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this manuscript, the authors utilized generative AI to refine the linguistic style, optimize the structural flow, and standardize bibliographic references to the AMA format. Following this process, the authors conducted a comprehensive manual review of the content to ensure scientific accuracy. The authors remain solely responsible for the substantive content of this publication, ensuring all findings are grounded in the analyzed peer-reviewed literature.

References

1. Pengelly M, Pumpa K, Pyne DB, Etxebarria N. Iron deficiency, supplementation, and sports performance in female athletes: a systematic review. *J Sport Health Sci.* 2024;14:101009. https://doi: 10.1016/j.jshs.2024.101009
2. Sim, M., Garvican-Lewis, L.A., Cox, G.R. *et al.* Iron considerations for the athlete: a narrative review. *Eur J Appl Physiol* 119, 1463–1478 (2019). https://doi.org/10.1007/s00421-019-04157-y
3. Kumar A, Sharma E, Marley A, Samaan MA, Brookes MJ. Iron deficiency anaemia: pathophysiology, assessment, practical management. *BMJ Open Gastroenterol*. 2022;9(1):e000759. https://doi:10.1136/bmjgast-2021-000759
4. Moisidis-Tesch, C.M., Shulman, L.P. Iron Deficiency in Women's Health: New Insights into Diagnosis and Treatment. *Adv Ther* 39, 2438–2451 (2022). https://doi.org/10.1007/s12325-022-02157-7
5. Pasricha SR, Tye-Din J, Muckenthaler MU, Swinkels DW. Iron deficiency. *Lancet*. 2021;397(10270):233-248. doi:10.1016/S0140-6736(20)32594-0
6. McCormick R, Sim M, Dawson B, Peeling P. Refining Treatment Strategies for Iron Deficient Athletes. *Sports Med*. 2020;50(12):2111-2123. https://doi:10.1007/s40279-020-01360-2
7. Nolte S, Maier C, Klügel S, et al. Menstrual blood loss as an initial trigger for adaptation of iron metabolism in eumenorrheic female athletes-An exploratory study. *Physiol Rep*. 2025;13(16):e70522. https://doi:10.14814/phy2.70522

8. Lippi G, Sanchis-Gomar F. Epidemiological, biological and clinical update on exercise-induced hemolysis. *Ann Transl Med*. 2019;7(12):270. https://doi:10.21037/atm.2019.05.41
9. Fazal AA, Whittemore MS, DeGeorge KC. Foot-strike haemolysis in an ultramarathon runner. *BMJ Case Rep*. 2017;2017:bcr2017220661. Published 2017 Dec 13. https://doi:10.1136/bcr-2017-220661
10. Sumi D and Suzuki Y (2025) Gastrointestinal function and microbiota in endurance athletes. Front. Physiol. 16:1551284. doi: 10.3389/fphys.2025.1551284
11. Kardasis W, Naquin ER, Garg R, et al. The IRONy in Athletic Performance. *Nutrients*. 2023;15(23):4945. Published 2023 Nov 28. https://doi:10.3390/nu15234945
12. McKay AKA, Pyne DB, Burke LM, Peeling P. Iron Metabolism: Interactions with Energy and Carbohydrate Availability. Nutrients. 2020; 12(12):3692. https://doi.org/10.3390/nu12123692
13. Dugan, C., Peeling, P., Burden, R. *et al.* Efficacy of iron supplementation on physical capacity in non-anaemic iron-deficient individuals: protocol for an individual patient data meta-analysis. *Syst Rev* 13, 182 (2024). https://doi.org/10.1186/s13643-024-02559-4
14. Lewis JL. Iron Deficiency Anemia. *MSD Manual Professional Version*. Updated October 2023. Accessed February 28, 2026. https://www.msdmanuals.com/professional/hematology-and-oncology/anemias-caused-by-deficient-erythropoiesis/iron-deficiency-anemia
15. Beard JL, Connor JR. Iron status and neural functioning. *Annu Rev Nutr*. 2003;23:41-58. doi:10.1146/annurev.nutr.23.020102.075739
16. Todorich B, Pasquini JM, Garcia CI, Paez PM, Connor JR. Oligodendrocytes and myelination: the role of iron. *Glia*. 2009;57(5):467-478. https://doi:10.1002/glia.20784
17. Gao Q, Zhou Y, Chen Y, et al. Role of iron in brain development, aging, and neurodegenerative diseases. *Ann Med*. 2025;57(1):2472871. https://doi:10.1080/07853890.2025.2472871
18. Fiani D, Kim JW, Hu M, et al. Iron Deficiency Without Anemia and Reduced Basal Ganglia Iron Content in Youths. *JAMA Netw Open*. 2025;8(6):e2516687. Published 2025 Jun 2. https://doi:10.1001/jamanetworkopen.2025.16687

19. Blanton, Cynthia & Green, Michael & Kretsch, Mary. (2012). Body iron is associated with cognitive executive planning function in college women. The British journal of nutrition. 109. 1-8.https://doi:10.1017/S0007114512002620
20. Dugan C, Simpson A, Peeling P, et al. The Perceived Impact of Iron Deficiency and Iron Therapy Preference in Exercising Females of Reproductive Age: A Cross-Sectional Survey Study. *Patient Prefer Adherence*. 2023;17:2097-2108. Published 2023 Aug 24. https://doi:10.2147/PPA.S397122
21. Murray-Kolb LE, Beard JL. Iron treatment normalizes cognitive functioning in young women. *Am J Clin Nutr*. 2007;85(3):778-787. https://doi:10.1093/ajcn/85.3.778
22. Greig AJ, Patterson AJ, Collins CE, Chalmers KA. Iron deficiency, cognition, mental health and fatigue in women of childbearing age: a systematic review. *J Nutr Sci*. 2013;2:e14. Published 2013 Apr 29. https://doi:10.1017/jns.2013.7
23. Stugiewicz M, Tkaczyszyn M, Kasztura M, Banasiak W, Ponikowski P, Jankowska EA. The influence of iron deficiency on the functioning of skeletal muscles: experimental evidence and clinical implications. *Eur J Heart Fail*. 2016;18(7):762-773. https://doi:10.1002/ejhf.467
24. Burden RJ, Morton K, Richards T, Whyte GP, Pedlar CR. Is iron treatment beneficial in, iron-deficient but non-anaemic (IDNA) endurance athletes? A systematic review and meta-analysis. *Br J Sports Med*. 2015;49(21):1389-1397. https://doi:10.1136/bjsports-2014-093624
25. Shaw G, Lee-Barthel A, Ross ML, Wang B, Baar K. Vitamin C-enriched gelatin supplementation before intermittent activity augments collagen synthesis. *Am J Clin Nutr*. 2017;105(1):136-143. https://doi.org/10.3945/ajcn.116.138594
26. Stoffel NU, Zeder C, Brittenham GM, Moretti D, Zimmermann MB. Iron absorption from supplements is greater with alternate day than with consecutive day dosing in iron-deficient anemic women. *Haematologica*. 2020;105(5):1232-1239. https://doi.org/10.3324/haematol.2019.220830
27. Moretti D, Goede JS, Zeder C, et al. Oral iron supplements increase hepcidin and decrease iron absorption from daily or twice-daily doses in iron-depleted young women. *Blood*. 2015;126(17):1981-1989. https://doi.org/10.1182/blood-2015-05-642223

28. Gattermann N, Muckenthaler MU, Kulozik AE, Metzgeroth G, Hastka J. The Evaluation of Iron Deficiency and Iron Overload. *Dtsch Arztebl Int*. 2021;118(49):847-856. https://doi:10.3238/arztebl.m2021.0290
29. Barney DE, Ippolito JR, Berryman CE, Hennigar SR. A Prolonged Bout of Running Increases Hepcidin and Decreases Dietary Iron Absorption in Trained Female and Male Runners. *J Nutr*. 2022;152(9):2039-2047. https://doi.org/10.1093/jn/nxac129
30. Šmid AN, Golja P, Hadžić V, Abazović E, Drole K, Paravlic AH. Effects of Oral Iron Supplementation on Blood Iron Status in Athletes: A Systematic Review, Meta-Analysis and Meta-Regression of Randomized Controlled Trials. *Sports Med*. 2024;54(5):1231-1247. https://doi.org/10.1007/s40279-024-01992-8
31. Govus AD, Garvican-Lewis LA, Abbiss CR, Peeling P, Gore CJ. Pre-Altitude Serum Ferritin Levels and Daily Oral Iron Supplement Dose Mediate Iron Parameter and Hemoglobin Mass Responses to Altitude Exposure. *PLoS One*. 2015;10(8):e0135120. Published 2015 Aug 11. https://doi.org/10.1371/journal.pone.0135120
32. Olszok M, Wijas D, Kluś M, et al. Subclinical Iron Deficiency in Athletes - Diagnostics, Consequences, and Management Strategies: A Narrative Review. *Journal of Education, Health and Sport*. 2026;88:69380. https://doi.org/10.12775/JEHS.2026.88.69380
33. Muszkieta R, Napierała M, Żukow W, et al. The impact of health-promoting behavior on the quality of life of football players. *Quality in Sport*. 2024;13:60804. https://doi.org/10.12775/QS.2025.42.60804
34. Schröder S, Frenkel J. Self-regulation skills and stress management during early sportschool-career. *Pedagogy and Psychology of Sport*. 2025;11:67572. https://doi.org/10.12775/PPS.2025.28.67572