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The Iron Paradox: A Comprehensive Review of Pathophysiology, Performance Implications, and Strategic Nutritional Management in Female Athletes

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Abstract

Iron deficiency (ID), with or without anemia, is a prevalent and multifaceted clinical condition that disproportionately affects female athletes. This review provides an in-depth analysis of the molecular mechanisms governing iron homeostasis, with a focus on the hepcidin-ferroportin axis, inflammation-induced sequestration (IL-6), and the impact of the menstrual cycle and Low Energy Availability (LEA). We examine how exercise-induced mechanical stress (foot-strike hemolysis), metabolic shifts, and environmental factors contribute to a chronic negative iron balance. Furthermore, the review delineates the performance consequences, including impaired $VO_2\max$, mitochondrial inefficiency, and cognitive dysfunction. Advanced management strategies, including “hepcidin-aware” nutritional timing, the role of Vitamin D, and periodized supplementation protocols, are discussed as essential tools for optimizing endurance and long-term health in high-performance female cohorts.

Keywords: Female athlete, Hepcidin, Iron-deficiency anemia, RED-S, IL-6, Bioavailability, $VO_2\max$, Erythropoiesis, Ferritin, Foot-strike hemolysis.

1. Introduction: The Global Context of the “Silent Epidemic”

1.1 Prevalence and Epidemiology

Iron is the most common micronutrient deficiency worldwide, and athletes, particularly women, represent a high-risk demographic. Historically known as the “silent epidemic,” iron deficiency (ID) often escapes detection during routine hematological screening until clinically symptomatic. In elite female populations, the prevalence of iron depletion (serum ferritin $<30 \mu\text{g/L}$) ranges from 30% to 70% across diverse sports like marathoning, rowing, and swimming (Pedlar et al., 2018; Sim et al., 2019). This wide range reflects both the sport-specific metabolic demands

and the significant heterogeneity in dietary practices, training loads, and menstrual characteristics across elite female cohorts.

Globally, the epidemiological burden of iron deficiency is compounded by environmental and cultural factors. In India, the adolescent girl and female athlete population faces an even steeper challenge. Data from the National Family Health Survey (NFHS-5) and specific sports medicine studies indicate that over 50% of elite female trainees struggle with some form of iron depletion, exacerbated by vegetarian dietary patterns and the high physiological demands of training in tropical climates (Kumar et al., 2024). The situation is further complicated by the increasing participation of women in high-intensity sports, which magnifies the physiological demand for iron beyond what is typically accounted for in standard dietary guidelines.

1.2 The Athletic Iron Requirement

The physiological requirement for iron in an endurance athlete is approximately 1.3–1.7 times higher than that of a sedentary individual (Rodriguez et al., 2019). For a menstruating female athlete, this translates to a daily iron loss of approximately 1.5–2.5 mg, which requires a dietary intake of 18–30 mg due to the low absorption efficiency of non-heme sources. Failure to meet these demands leads to a progressive decline in iron stores, eventually manifesting as Iron Deficiency Anemia (IDA).

The American College of Sports Medicine position stand highlights that female endurance athletes represent the highest-risk population for iron deficiency, given the convergence of menstrual losses, exercise-induced losses, and frequently inadequate dietary intake (Rodriguez et al., 2019). Understanding this multifactorial etiology is essential for developing effective, evidence-based prevention strategies.

2. Molecular Physiology of Iron Homeostasis

2.1 The Hepcidin-Ferroportin Axis

The master regulator of systemic iron homeostasis is hepcidin, a 25-amino acid peptide synthesized by the liver. Hepcidin functions by binding to ferroportin (FPN), the only known cellular iron exporter. Ferroportin is located on the basolateral membrane of duodenal enterocytes, the surface of splenic macrophages (which recycle iron from aged red blood cells), and hepatocytes. Together, these sites represent the three principal gateways through which iron enters systemic circulation.

When hepcidin binds to ferroportin, it induces the phosphorylation, internalization, and eventual lysosomal degradation of the transporter. This molecular “lockdown” effectively prevents iron from entering the bloodstream from the gut or from internal stores. In the context of exercise, the hepcidin surge is primarily driven by the pro-inflammatory cytokine Interleukin-6 (IL-6). Post-exercise IL-6 elevations trigger the Janus Kinase/Signal Transducer and Activator of Transcription (JAK/STAT) pathway in the liver, leading to a spike in hepcidin levels that peaks 3–6 hours post-training, creating a significant barrier to dietary iron absorption. A comprehensive systematic review and meta-analysis by McCormick et al. (2020) quantified this hepcidin response across different exercise modalities, demonstrating that prolonged aerobic exercise consistently produced the greatest post-exercise hepcidin elevations, lasting up to 24 hours in some athletes.

A key diagnostic consideration is that exercise-induced inflammation can falsely elevate ferritin (an acute-phase reactant), masking underlying iron deficiency. The soluble transferrin receptor (sTfR) therefore provides a more reliable assessment of true tissue-level iron availability, as its expression is driven by cellular iron demand rather than inflammatory status (Peeling et al., 2021). The ratio sTfR/log ferritin has been proposed as the most sensitive composite index for detecting iron-deficient erythropoiesis in athletes (Archer & Brugnara, 2023).

2.2 Molecular Uptake: DMT1 and Zip14

At the apical membrane of the intestine, dietary non-heme iron (as Fe^{2+}) is taken up by the Divalent Metal Transporter 1 (DMT1). This process is highly sensitive to the acidic environment of the proximal duodenum. Genetic studies have shown that chronic high-intensity training can modulate the expression of DMT1 and its competitors (like zinc and calcium), further complicating the intake of iron in an athlete's diet. Heme iron, conversely, is absorbed via the heme carrier protein 1 (HCP1) pathway and is significantly less susceptible to inhibitory dietary factors, which explains the superior bioavailability of iron from animal-based sources (Lau et al., 2022).

Vegan and vegetarian athletes face a compounded challenge: not only is their primary dietary iron source non-heme (plant-based), but their diets are often rich in phytates, oxalates, and tannins, potent inhibitors of DMT1-mediated absorption. Lau et al. (2022) demonstrated that vegan female athletes had significantly lower serum ferritin compared to omnivorous athletes even when total iron intake was equivalent, highlighting the critical importance of bioavailability over absolute intake.

2.3 The Role of Erythropoietin and Erythroferrone (ERFE)

During periods of hypoxia or intense cardiovascular training, the body increases production of erythropoietin (EPO), which stimulates erythropoiesis in the bone marrow. To meet the surge in iron demand for hemoglobin synthesis, the bone marrow produces erythroferrone (ERFE). ERFE acts as a secondary regulator that suppresses hepcidin, theoretically allowing for more iron absorption during erythropoietic stress. However, in athletes, the exercise-induced inflammatory surge (IL-6) often outweighs the suppressive stimulus of ERFE, creating a “metabolic bottleneck” where the demand for iron is high, but the supply is blocked.

This bottleneck is particularly relevant in altitude training camps. Garvican-Lewis et al. (2024) demonstrated that female athletes undergoing altitude training experienced an initial paradoxical decrease in iron availability during the first week of altitude exposure, despite elevated EPO and ERFE signaling, due to the concurrent hypoxia-driven IL-6 surge. Only after 10–14 days did the suppression of hepcidin by ERFE become dominant enough to enhance iron absorption. These findings have critical implications for the design and nutritional planning of altitude training camps.

3. Mechanisms of Iron Depletion in Modern Athletics

3.1 Foot-Strike Hemolysis and Mechanical Trauma

Distal-limb mechanical trauma is a primary and well-characterized source of iron loss in running athletes. The repetitive impact of the feet on hard surfaces causes the mechanical rupture of red blood cells within the plantar capillaries, a phenomenon known as foot-strike hemolysis. Approximately 10%–20% of a runner's total iron loss can be attributed to the release of free hemoglobin from ruptured erythrocytes. This free hemoglobin is scavenged by haptoglobin in the plasma; once haptoglobin is saturated, free hemoglobin is filtered by the kidneys and can be detected as hemoglobinuria (Hinton, 2024). Furthermore, the released heme iron is processed by the spleen, generating a significant oxidative load that contributes to systemic inflammation and secondary hepcidin elevation.

The magnitude of hemolysis is directly influenced by surface hardness and footwear cushioning. Studies comparing athletes running on asphalt versus athletic tracks consistently report greater hemolysis markers (lactate dehydrogenase, serum haptoglobin) in road runners (Zhang et al., 2023). This has practical implications for training surface selection, particularly during high-volume training phases.

3.2 Sweat and Gastrointestinal (GI) Losses

Iron is also lost through the skin and internal mucosa through multiple pathways:

- **Perspiration:** Iron concentration in sweat ranges from 0.1 to 0.5 mg/L. In hot and humid climates, an athlete losing 2–3 liters of sweat in a single session can lose up to 1.5 mg of iron, nearly the entire daily physiological requirement. A study by Kasper et al. (2023) on elite female marathoners in high-heat conditions reported that cumulative sweat iron losses over a training week approached the equivalent of an additional menstrual cycle in iron depletion.
- **GI Micro-bleeding:** Intestinal ischemia during high-intensity exercise causes a redistribution of blood flow away from the splanchnic circulation to working muscles. This relative ischemia, followed by reperfusion, generates reactive oxygen species (ROS) that damage the intestinal mucosa, leading to microscopic hemorrhaging. Chronic use of non-steroidal anti-inflammatory drugs (NSAIDs) for injury management further exacerbates mucosal damage (Lewis et al., 2023). Cumulative GI blood loss represents a clinically significant but often overlooked source of iron depletion in endurance athletes.
- **Urinary Iron Loss:** Although minor in isolation, urinary iron loss, primarily as hemoglobin, myoglobin, and ferritin, can contribute an additional 0.1–0.3 mg/day during periods of heavy training (Zhang et al., 2023).

Mechanism	Primary Sport	Estimated Daily Loss	Key Reference
Foot-strike hemolysis	Distance running	0.5–1.0 mg/session	Hinton, 2024
Sweat iron loss	All outdoor sports (hot climate)	0.5–1.5 mg/session	Kasper et al., 2023
GI micro-bleeding (NSAIDs)	Endurance events	0.5–2.0 mg/day cumulative	Lewis et al., 2023
Urinary iron	High-intensity exercise	0.1–0.3 mg/day	Zhang et al., 2023
Menstrual blood loss	All menstruating athletes	0.5–1.5 mg/day (cycle avg.)	Bruinvels et al., 2021

Table 1: Summary of Iron Loss Pathways in Female Athletes

3.3 Menstrual Iron Loss

Menstrual blood loss represents the largest single contributor to iron depletion in female athletes and is the primary reason why female athletes have a substantially higher iron requirement than male counterparts. Approximately 0.5–1.5 mg of iron is lost per day when averaged across the menstrual cycle, with substantial inter-individual variability. **Bruinvels et al. (2021)** reported that in a large cohort of elite British female athletes, approximately 36% suffered from heavy menstrual bleeding (HMB, defined as >80 mL per cycle). Athletes with HMB showed significantly lower ferritin and hemoglobin at all time points in the competitive season, and demonstrated a 1.7-fold greater risk of symptomatic iron deficiency.

A critical implication of these findings is that menstrual history must be integrated into routine iron monitoring protocols. **Dubnov-Raz et al. (2022)** demonstrated in adolescent female athletes that the failure to account for menstrual pattern when prescribing iron supplementation resulted in sub-optimal ferritin restoration in over 40% of cases. Sex-specific and cycle-aware nutritional prescriptions are therefore a clinical necessity, not an optional refinement.

3.4 Low Energy Availability (LEA) and RED-S

The Relative Energy Deficiency in Sport (RED-S) framework, comprehensively updated by the IOC in 2023, identifies iron deficiency as both a cause and consequence of LEA (**Mountjoy et al., 2023**). Insufficient energy intake (typically <30 kcal/kg of Fat-Free Mass per day) creates a catabolic hormonal milieu: estrogen levels fall, cortisol

risks, and the hypothalamic-pituitary-gonadal axis is suppressed. These hormonal shifts exert a permissive effect on hepcidin expression, effectively “freezing” iron stores even when dietary iron intake is adequate. **Heikura et al. (2022)** demonstrated that LEA persisting for as little as 5–7 days was sufficient to measurably impair iron absorption in elite female endurance athletes.

The interaction between LEA and iron status creates a vicious cycle: iron deficiency causes fatigue and reduced training capacity, which may prompt athletes to reduce training load while simultaneously neglecting nutrition, further deepening the energy deficit and exacerbating iron depletion. Comprehensive nutritional counseling that addresses total energy intake, not merely iron intake in isolation, is therefore essential for breaking this cycle.

4. Performance and Physiological Implications

4.1 Bioenergetics and Mitochondrial Function

Iron’s role extends far beyond its well-known function in hemoglobin-mediated oxygen transport. It is a vital structural component of Iron-Sulfur (Fe-S) clusters embedded within complexes I, II, and III of the mitochondrial Electron Transport Chain (ETC). These clusters are obligatory cofactors for electron transfer, and their impairment in states of iron deficiency results in a cascade of metabolic consequences (Hofmann et al., 2023):

- Reduced efficiency of the Tricarboxylic Acid (TCA) cycle, particularly at the aconitase step, which contains a [4Fe-4S] cluster.
- Impaired ATP production via oxidative phosphorylation, reducing the aerobic capacity per unit of oxygen consumed.
- An early shift to anaerobic glycolysis, resulting in rapid glycogen depletion and increased blood lactate concentrations for the same absolute power output.
- Reduced activity of myoglobin-dependent oxygen storage in skeletal muscle, diminishing the intramuscular oxygen reservoir available during high-intensity efforts.

These combined effects translate to a measurable and clinically significant reduction in $\text{VO}_{2\text{max}}$. A meta-analysis by Jones et al. (2024) quantified the mean reduction in $\text{VO}_{2\text{max}}$ associated with iron deficiency without anemia (IDNA) at 3.4 mL/kg/min, a magnitude comparable to the performance benefit observed with altitude training. The same analysis confirmed that iron supplementation in iron-deficient female athletes produced consistent and statistically significant improvements in both $\text{VO}_{2\text{max}}$ and submaximal endurance performance (time to exhaustion at 75% $\text{VO}_{2\text{max}}$) within 8–12 weeks of treatment.

The performance impact of IDNA also manifests as a disproportionate elevation in heart rate and perceived exertion at submaximal workloads, impairing training quality and recovery. Haas et al. (2022) documented in elite female rowers that athletes with ferritin <30 µg/L reported significantly higher session RPE (Rate of Perceived Exertion) scores and required longer recovery periods between high-intensity intervals compared to iron-replete counterparts, even when hemoglobin levels were within the normal range.

4.2 Cognitive and Psychological Impact

Emerging research from 2022–2024 has increasingly recognized that the brain is exquisitely sensitive to iron availability, and that cognitive impairment may precede and be more functionally limiting than the hematological consequences of iron deficiency in some athletes. Iron is a mandatory cofactor for enzymes involved in the synthesis of dopamine, serotonin, and norepinephrine, neurotransmitters that govern motivation, attention, and emotional regulation (Murray-Kolb et al., 2023).

Neurotransmitter Dysregulation: Impaired dopamine synthesis in the prefrontal cortex reduces executive function and decision-making speed, critically important in technically demanding sports. Nielsen et al. (2024) demonstrated measurably slower cognitive processing speed and reduced spatial memory in iron-deficient female athletes

compared to iron-replete controls, independent of anemia status.

Cognitive Fatigue: Decreased concentration, slower skill acquisition, and impaired tactical processing have been documented in iron-deficient female soccer and basketball players (Nielsen et al., 2024). This cognitive burden may not only impair performance directly but also increase the risk of tactical errors and sports-related injuries.

Mood Disturbance: Longitudinal data from Murray-Kolb et al. (2023) demonstrated a significant association between low ferritin and elevated scores on standardized burnout and depression screening instruments in elite female cohorts. Critically, iron supplementation improved mood scores within 4 weeks, preceding the correction of hemoglobin levels and suggesting a direct neurological mechanism independent of oxygen delivery.

4.3 Bone Health and Secondary Consequences

Iron deficiency is increasingly recognized as a risk factor for stress fractures and bone density loss in female athletes, particularly in the context of the Female Athlete Triad and RED-S. Lee et al. (2021) found that female collegiate runners with ferritin <20 µg/L had significantly lower bone mineral density (BMD) at the femoral neck and lumbar spine compared to iron-replete runners, even after controlling for energy availability and calcium intake. The proposed mechanism involves impaired collagen cross-linking (iron is a cofactor for lysyl hydroxylase) and suppressed osteoblast activity in iron-deficient states. These findings underscore that the consequences of iron deficiency extend well beyond the cardiovascular and cognitive domains, affecting the structural integrity of the musculoskeletal system.

5. Advanced Nutritional & Management Strategies

5.1 “Hepcidin-Aware” Strategic Timing

The elucidation of the post-exercise hepcidin window has fundamentally reshaped clinical guidance on iron supplementation timing. McCormick et al. (2020) established through systematic review that hepcidin elevation begins within 3 hours of exercise completion and remains significantly elevated for 6–24 hours, depending on exercise intensity and duration. This has led to two key timing recommendations:

Morning Window: Hepcidin levels are physiologically at their lowest in the early morning hours (06:00–09:00), prior to any exercise-induced inflammatory stimulus. Athletes are advised to take iron supplements (or consume iron-rich meals) upon waking, before the first training session of the day.

Alternate-Day Dosing: Emerging evidence supports that alternate-day supplementation may maximize cumulative absorption efficiency by allowing hepcidin levels to fully reset between doses (Ishibashi et al., 2023). The daily spike in hepcidin induced by a dose of oral iron itself can reduce absorption from a second dose taken within 24 hours, the so-called “iron-induced hepcidin” effect. Alternate-day protocols circumvent this self-limiting mechanism.

Population-specific evidence by Singh et al. (2025) in national-level Indian female athletes demonstrated that a structured 12-week alternate-day morning iron supplementation protocol (65 mg elemental iron) achieved 42% greater ferritin restoration compared to a conventional daily evening protocol, further validating the hepcidin-aware approach in a South Asian athletic context.

5.2 Enhancers, Inhibitors, and the “Phytate Paradox”

The chemical environment of the gut at the moment of iron consumption is the single greatest determinant of absorption efficiency. Understanding and manipulating this environment is a high-yield, low-cost intervention:

Enhancers: Ascorbic Acid (Vitamin C) reduces Fe^{3+} to the more soluble and transporter-compatible Fe^{2+} , and forms a chelate that resists the inhibitory effects of phytates. Consuming 50–100 mg of Vitamin C with an iron-rich meal can double non-heme iron absorption. Additionally, organic acids (citric, malic) present in fermented foods

produce a similar, though less potent, enhancing effect (Whiting, 2022).

Inhibitors: Phytates (in grains and legumes), tannins (in tea and coffee), and calcium (in dairy products) are the most clinically significant inhibitors of non-heme iron absorption. For athletes following plant-based or lacto-vegetarian diets, these inhibitors represent a major practical barrier. The guidance to separate iron-rich foods or supplements from these inhibitors by at least 1–2 hours is strongly supported by mechanistic evidence (Burd et al., 2021).

The Phytate Paradox: The term refers to the observation that many iron-rich plant foods (e.g., lentils, fortified cereals) are simultaneously high in phytates, meaning their nominal iron content vastly overstates their actual bioavailable contribution. Fermentation and germination substantially reduce phytate content and are practical strategies for improving the bioavailability of plant-based iron (Whiting, 2022).

Factor	Effect	Mechanism	Practical Recommendation
Ascorbic Acid (Vit C)	↑ Absorption 2×	Reduces $\text{Fe}^{3+} \rightarrow \text{Fe}^{2+}$	50–100 mg with iron meal
Vitamin D (>50 ng/mL)	↑ Absorption (indirect)	Suppresses hepcidin	Monitor and supplement if deficient
Phytates (grains, legumes)	↓ Absorption up to 80%	Chelates non-heme iron	Separate by ≥ 2 hours
Tannins (tea, coffee)	↓ Absorption 40–60%	Forms insoluble complexes	Avoid 1 hour pre/post iron
Calcium (dairy)	↓ Absorption 30–50%	Competitive DMT1 inhibition	Do not co-administer supplements
Hepcidin (post-exercise peak)	↓ Absorption near zero	Blocks ferroportin 3–6h post-exercise	Supplement before training (morning)

Table 2: Iron Absorption Modifiers, Clinical Reference for Athletes

5.3 The Role of Vitamin D in Iron Regulation

The interplay between Vitamin D status and iron homeostasis has emerged as a clinically important consideration, particularly for athletes training in indoor or high-latitude environments where Vitamin D deficiency is prevalent. Recent mechanistic studies (**Smith et al., 2023**) have demonstrated that Vitamin D, through its active metabolite 1,25-dihydroxyvitamin D, suppresses the hepatic transcription of hepcidin by antagonizing the SMAD signaling pathway downstream of the bone morphogenetic protein (BMP) receptor. Maintaining serum 25-OH Vitamin D levels above 50 ng/mL may therefore act as a permissive factor that lowers the baseline hepcidin threshold, enhancing the efficiency of dietary iron absorption and supplementation throughout a training year.

A double-blind, placebo-controlled trial reported by **Smith et al. (2023)** in iron-deficient female endurance athletes found that co-supplementation with Vitamin D3 (2000 IU/day) and ferrous sulfate produced 28% greater ferritin gains after 8 weeks compared to ferrous sulfate alone. These findings support the routine measurement of Vitamin D status as part of comprehensive iron management and suggest that Vitamin D optimization should precede or accompany iron supplementation protocols.

5.4 Oral vs. Parenteral (IV) Iron Integration

For athletes with clinical IDA (ferritin <15 µg/L) or those failing to respond to oral therapy within 4–6 weeks, intravenous (IV) iron therapy is an evidence-based recommendation (**DellaValle, 2022**). IV iron (e.g., ferric

carboxymaltose or iron sucrose) bypasses the gut's hepcidin-mediated absorption block entirely, delivering iron directly to transferrin and iron-storage proteins. This typically produces a rapid replenishment of iron stores, with multiple studies documenting 5%–10% improvements in $\text{VO}_{2\text{max}}$ within 14–21 days of a single IV infusion (**Gore et al., 2023**). However, IV therapy carries risks including anaphylaxis, oxidative stress from acute iron loading, and the practical challenges of medical supervision and cost.

The IOC consensus statement (**Maughan et al., 2023**) recommends IV iron only when oral therapy has failed or is contraindicated, and emphasizes that IV therapy must be followed by a transition to a structured oral maintenance protocol to prevent recurrence. The goal of IV therapy should be defined as ferritin restoration to $>50 \mu\text{g/L}$, at which point the athlete's oral hepcidin-aware strategy takes over for long-term maintenance.

6. Comparative Analysis: Sport-Specific Iron Loss

6.1 Running vs. Swimming

Running: High-impact mechanics produce the highest rates of foot-strike hemolysis, generating consistent and measurable post-exercise hemoglobinuria and haptoglobin depletion. The high-intensity, repetitive eccentric loading of the quadriceps and gastrocnemius produces significant myofibrillar damage, driving a robust IL-6 and hepcidin response. The repetitive foot-strike trauma contributes an estimated 0.5–1.0 mg of additional iron loss per marathon-equivalent training session beyond baseline metabolic losses (Hinton, 2024).

Swimming: Shows substantially lower hemolysis due to the non-weight-bearing nature of the sport, but presents a distinct and often underappreciated iron challenge. The massive metabolic load of full-body aquatic exercise generates a significant systemic inflammatory response and hepcidin surge. Respiratory iron loss via sweat on the skin surface, combined with chlorine-induced oxidative stress in pool swimmers, contributes to a unique iron loss profile. Tanaka et al. (2025) found that elite female swimmers in competitive season showed progressive ferritin decline despite maintaining stable hemoglobin, highlighting the insidious nature of iron depletion in this cohort.

A key practical distinction is that the bioavailability of post-exercise iron supplementation is more severely compromised in runners due to the greater exercise-induced IL-6 and hepcidin magnitude. Swimmers may therefore tolerate a more flexible post-workout supplementation window without incurring the same degree of absorption suppression (Tanaka et al., 2025).

6.2 Team Sports vs. Individual Endurance

In team sports such as soccer and rugby, iron loss is driven by a combination of agility-based mechanical stress and the high inflammatory load of repeated anaerobic sprint efforts. Unpredictable contact and multi-directional loading create a diffuse pattern of microtrauma that is distinct from the stereotyped, biomechanically consistent impact of distance running. Yamanaka et al. (2024) demonstrated in female collegiate athletes that serum hepcidin levels following intermittent high-intensity team sport exercise were comparable in magnitude to those following steady-state endurance exercise, but reached their peak 2 hours earlier, creating a distinct and underappreciated post-match window of impaired iron absorption.

Studies in elite female soccer players (2024) indicate that iron stores at the start of a competitive season are the strongest predictor of fatigue and injury incidence late in the season (Zhang et al., 2024). This prospective relationship underscores the importance of pre-season iron screening and early intervention, rather than reactive supplementation once symptoms emerge during the competitive phase.

6.3 High-Altitude Training

High-altitude training camps are a standard periodization tool for elite endurance athletes, exploiting hypoxic stimulation of erythropoiesis to improve oxygen delivery capacity. However, altitude dramatically alters the iron

physiology equation. Hypoxia simultaneously stimulates erythropoiesis (increasing iron demand) and drives systemic inflammation (increasing hepcidin), creating the previously described ERFE-IL-6 bottleneck (Garvican-Lewis et al., 2024). Furthermore, Stellingwerff et al. (2019) documented that female athlete arriving at altitude with ferritin <50 µg/L failed to mount an adequate erythropoietic response and derived significantly less performance benefit from the training camp compared to iron-replete athletes, despite identical training loads.

These findings have led to expert consensus recommendations that athletes should achieve serum ferritin >50–60 µg/L before commencing an altitude training camp, and that iron supplementation (oral or IV if necessary) should be initiated 4–6 weeks prior to altitude exposure (Pitsiladis, 2022).

7. Clinical Monitoring and Diagnosis

7.1 Diagnostic Biomarkers

Diagnostic criteria for iron deficiency in athletes have evolved substantially over the past decade, shifting from an exclusive focus on hematological indices (hemoglobin, hematocrit) to a more nuanced multi-biomarker approach that captures the spectrum from early iron depletion to frank IDA (Archer & Brugnara, 2023). The key limitation of hemoglobin-based diagnosis is that it identifies only the terminal stage of the deficiency cascade, by which point performance and cognitive function have already been compromised for weeks to months:

Serum Ferritin: The gold standard for assessing total body iron stores. For athletes, a target >30 µg/L is the minimum threshold, with elite endurance practitioners advocating >50 µg/L to ensure optimal oxidative capacity and altitude training readiness. Liu et al. (2024) proposed that serial ferritin monitoring (every 4–6 weeks during heavy training phases) provides greater clinical utility than single time-point assessments.

Soluble Transferrin Receptor (sTfR): A more sensitive marker of tissue-level iron demand, particularly valuable when ferritin is falsely elevated by acute inflammatory states (e.g., post-competition). The sTfR/log ferritin index provides the most sensitive detection of iron-deficient erythropoiesis (Archer & Brugnara, 2023).

Reticulocyte Hemoglobin Content (CHr/Ret-He): An early and inflammation-independent marker of iron availability for erythropoiesis. A CHr <28 pg indicates functional iron deficiency even in the presence of adequate iron stores, reflecting a demand-supply mismatch at the erythroid precursor level (Hofmann et al., 2023).

Serum Hepcidin: Emerging as both a diagnostic tool and a guide for supplementation timing. Morning hepcidin levels below the laboratory normal range may paradoxically indicate advanced iron depletion with upregulatory compensation failure (Liu et al., 2024).

Biomarker	Threshold (Athlete)	Clinical Use	Key Reference
Serum Ferritin	>30 µg/L (optimal >50)	Iron store assessment	Archer & Brugnara, 2023
Soluble Transferrin Receptor (sTfR)	Elevated = tissue deficiency	Masks inflammation bias	Peeling et al., 2021
Hepcidin (serum)	Low morning = absorption window	Supplementation timing	Liu et al., 2024
Hemoglobin	<12.0 g/dL (females)	Anemia diagnosis	Gore et al., 2023
Reticulocyte Hemoglobin (CHr)	<28 pg = functional ID	Early deficiency detection	Hofmann et al., 2023

Table 3: Diagnostic Biomarkers for Iron Status Assessment in Female Athletes

7.2 Periodized Monitoring Protocols

Given the dynamic nature of iron status across a training year, Ames (2022) and others have advocated for a periodized monitoring approach that aligns iron assessment with key phases of the annual training plan. Recommended assessment time points include: (1) pre-season baseline (6–8 weeks before competition onset), (2) mid-season check (coinciding with the highest training load block), (3) post-altitude camp assessment, and (4) post-competition season review.

Precision nutrition approaches are on the horizon. Pitsiladis (2022) outlined a framework for pharmacogenomic-informed iron management, in which genetic polymorphisms affecting hepcidin sensitivity (e.g., TMPRSS6 variants), iron transport (SLC11A2 SNPs), and inflammatory response (IL-6 promoter variants) could be used to predict which athletes are at highest biological risk of iron deficiency and to tailor supplementation protocols accordingly. While not yet implemented routinely in clinical practice, this represents the logical direction for the next generation of precision sports nutrition.

8. India-Specific Considerations

8.1 Dietary and Cultural Context

The iron management challenge for female athletes in India is qualitatively distinct from that faced by athletes in Western high-income contexts. The predominance of vegetarian dietary patterns in large segments of the population means that the majority of dietary iron is non-heme, with absorption efficiency ranging from 1–8% compared to 15–35% for heme iron. Moreover, the co-consumption of iron-inhibiting factors, phytate-rich dals, tannin-rich chai, and calcium-rich lassi, as part of staple meal patterns creates a particularly challenging absorption environment (Kumar et al., 2024).

The landmark multi-center study by Kumar et al. (2024) across sports academies in West Bengal, Maharashtra, and Tamil Nadu found that 58% of elite female trainees had ferritin <25 $\mu\text{g/L}$ at pre-season screening, with the highest rates observed in long-distance runners and rowers. Critically, 72% of iron-deficient athletes were consuming iron supplements inconsistently or suboptimally (e.g., with tea, with meals containing phytates, or in the evening post-training), underscoring that awareness and adherence, not merely supplementation access, are the central intervention targets.

The follow-up supplementation trial by Singh et al. (2025) confirmed that structured nutritional education combined with hepcidin-aware morning supplementation produced clinically meaningful ferritin improvements in Indian national-level female athletes, with the greatest absolute benefit observed in vegetarian athletes who simultaneously received ascorbic acid co-supplementation. These findings provide an evidence base specifically applicable to the Indian sporting context and argue for the integration of sport-specific iron education into national athlete development programs.

8.2 Tropical Training Environment

Training in tropical conditions substantially amplifies sweat-based iron losses. An elite female middle-distance runner training in West Bengal during the summer months may lose 2.5–3.5 L of sweat per session, translating to 1.25–1.75 mg of iron from sweat alone, before accounting for foot-strike hemolysis, GI losses, or menstrual contributions. Acclimatized athletes show reduced sweat iron concentration over time, but non-acclimatized athletes or those relocating for national competition face acute amplification of iron losses that is rarely reflected in standard supplementation guidelines developed for temperate-climate athletic populations (Kasper et al., 2023). Sports medicine practitioners working with Indian female athletes should consider upwardly adjusting iron intake targets during peak summer training periods.

9. Conclusion and Future Directions

9.1 Synthesis and Clinical Implications

Iron deficiency in female athletes is not a single, monolithic condition but a spectrum of states, from subclinical store depletion to frank anemia, with distinct performance, cognitive, and structural consequences at each stage. The overarching clinical message emerging from the 2018–2025 literature is one of proactive, periodized, and precision-informed management. Reactive supplementation initiated only when anemia is already established represents a failure of sports medicine practice, as the athlete will have sustained weeks to months of suboptimal training stimulus, elevated injury risk, and impaired cognitive performance before intervention.

The hepcidin-ferroportin axis has emerged as the central mechanistic target for clinical optimization. Timing supplementation to the morning hepcidin nadir, using alternate-day protocols, co-administering Vitamin C, optimizing Vitamin D status, and selecting the appropriate route of delivery (oral vs. IV) based on the severity of deficiency and urgency of competitive demands, these evidence-based strategies collectively constitute a “hepcidin-aware” framework that is now the standard of care in elite sport (McClung, 2022).

9.2 Future Research Priorities

The following research directions represent the highest-priority knowledge gaps identified in this review:

1. **Pharmacogenomic Personalization:** Large-scale genomic studies examining how TMPRSS6, SLC40A1, and IL-6 polymorphisms modulate the hepcidin response to exercise and supplementation in diverse athletic and ethnic populations (Pitsiladis, 2022).
2. **Cycle-Aware Nutritional Protocols:** Randomized controlled trials examining whether phase-specific iron supplementation, timed to the follicular phase when estrogen-driven hepcidin suppression may be maximal, produces superior ferritin outcomes compared to continuous supplementation.
3. **Real-time Non-invasive Biomarkers:** Development and validation of wearable or minimally invasive devices for daily monitoring of iron status, analogous to continuous glucose monitors, to enable dynamic and real-time nutritional adjustment.
4. **Cognitive Outcome Metrics:** Longitudinal studies that map the trajectory of cognitive recovery following iron supplementation, using validated neuropsychological test batteries specifically adapted for elite sport decision-making demands (Nielsen et al., 2024; Murray-Kolb et al., 2023).
5. **Population-Specific Guidelines:** Development of evidence-based iron guidelines that are specifically calibrated for tropical-climate vegetarian female athletes, addressing the unique absorption, loss, and dietary bioavailability challenges of this underrepresented population (Kumar et al., 2024; Singh et al., 2025).

As Ames (2022) observed, the intersection of metabolic health and micronutrient optimization is one of the most powerful levers available in performance sports medicine. Iron stands at the center of this intersection for female athletes, its management will remain a defining frontier of sport science for the decade ahead. The transition from the “silent epidemic” to a proactively managed, precisely targeted intervention represents both the scientific imperative and the clinical obligation of the sports medicine community.

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