Immunopathologia Persa
DOI:10.34172/ipp.44062
http immunopathol.com

Iron deficiency and anemia in rheumatoid arthritis; pathophysiology, corticosteroid effects, and inflammatory mechanisms – a narrative review study

Wida Simzari*

Department of Nutrition and Dietetics, Faculty of Health Sciences, Istanbul Nişantaşı University, Istanbul, Türkiye

***Correspondence to**
Wida Simzari, Email: wida.simzari@nisantasi.edu.tr

Received 18 May. 2026
Revised: 27 Jun. 2026
Accepted 1 Jul. 2026
ePublished 9 Jul. 2026

Keywords: Rheumatoid arthritis, Anemia of chronic disease, Anemia of inflammation, Iron deficiency, Hepcidin, Ferroportin, Interleukin-6, Corticosteroids, Tocilizumab

Abstract

Anemia is a common and clinically significant extra-articular complication of rheumatoid arthritis (RA), driven by multifactorial mechanisms including anemia of inflammation and coexisting iron deficiency anemia (IDA), which complicate diagnosis. Proinflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) promote hepcidin overproduction, leading to iron sequestration, reduced absorption, impaired erythropoiesis, and shortened erythrocyte survival, alongside suppressed erythropoietin (EPO) activity. Corticosteroids exert bidirectional effects, offering short-term improvement but potentially disrupting long-term hematopoiesis. Diagnosis is challenging due to inflammation-related elevations in ferritin, whereas soluble transferrin receptor (sTfR) provides greater accuracy. Targeting inflammation with disease-modifying antirheumatic drugs (DMARDs) and biologics, particularly tocilizumab (TCZ), effectively improves anemia. This narrative review synthesizes evidence from randomized controlled trials and cohort studies over the past decades, evaluating the pathophysiology, diagnostic challenges, corticosteroid interactions, and therapeutic approaches to anemia in RA to provide clinicians with a comprehensive, evidence-based framework for management.

Citation: Simzari W. Iron deficiency and anemia in rheumatoid arthritis; pathophysiology, corticosteroid effects, and inflammatory mechanisms – a narrative review study. Immunopathol Persa. 2026;x(x):e44062. DOI:10.34172/ipp.44062.

Introduction

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disorder defined by persistent synovitis, progressive joint destruction, and a broad spectrum of extra-articular manifestations that collectively impose a substantial burden on affected individuals and healthcare systems alike (1-4). The disease is characterized by immune-mediated inflammatory processes that extend well beyond the articular compartment, engaging multiple organ systems and predisposing patients to a range of comorbidities, including osteoporosis, cardiovascular disease, and hematological abnormalities (5,6). Among the systemic complications of RA, anemia stands out as both highly prevalent and clinically consequential, yet it frequently remains underdiagnosed and inadequately treated in routine care (7).

Reported prevalence estimates for anemia in RA vary considerably depending on diagnostic criteria, patient population, and disease activity status, ranging from approximately 10% to over 55% in different studies (8-10). A cross-sectional analysis of 330 RA patients conducted across three tertiary care centers found anemia in 54.55% of participants, with mean hemoglobin levels of 11.41 ± 1.87 g/dL in affected individuals (9). Anemia in RA is significantly associated with higher disease activity scores, elevated inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), and longer disease duration, making it both a marker of disease severity and an independent contributor to poor outcomes (9, 11). A population-based analysis using the National Health and Nutrition Examination Survey (NHANES) database, spanning 20 years from 1999 to 2018, estimated the prevalence of anemia in RA patients in the United States at approximately 10.25%, with a characteristic U-shaped distribution across age groups, lowest around 60 years of age, and a modestly higher prevalence in females compared to males (8).

The presence of anemia in RA carries important prognostic implications beyond its symptomatic burden. Retrospective cohort studies have demonstrated that anemia is associated with progression in RA, suggesting it reflects the intensity of systemic inflammation that simultaneously damages articular structures (12). The overlap between different anemia subtypes in RA, particularly

Key point

The literature review indicated that anemia is a frequent extra-articular manifestation of rheumatoid arthritis (RA), primarily driven by inflammation-mediated mechanisms and often accompanied by iron deficiency anemia (IDA), complicating its diagnosis. Proinflammatory cytokines, particularly interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) stimulate hepcidin overproduction, resulting in disrupted iron homeostasis, impaired erythropoiesis, and reduced erythrocyte lifespan. Corticosteroids exert variable effects, offering short-term hematologic improvement through anti-inflammatory action, but potentially contributing to long-term dysregulation. Diagnostic assessment is further complicated by the limited reliability of ferritin as an acute-phase reactant, whereas soluble transferrin receptor (sTfR) provides greater diagnostic accuracy under inflammatory conditions. Therapeutic approaches targeting inflammation, including disease-modifying antirheumatic drugs (DMARDs) and biologic agents such as tocilizumab (TCZ), have demonstrated effectiveness in ameliorating anemia. The Mediterranean diet can also alleviate iron deficiency by dampening IL-6–driven hepcidin upregulation via its anti-inflammatory phytochemicals and omega-3 fatty acids, and by improving non-heme iron absorption through its vitamin C–rich plant foods.

anemia of inflammation and true iron deficiency anemia (IDA), complicates both diagnosis and treatment, requiring careful evaluation of iron metabolism parameters within the context of chronic inflammatory disease (7). The present narrative review synthesizes current evidence from controlled trials and cohort studies published over the past decades, examining the pathophysiology of anemia in RA with a focus on inflammatory mechanisms, the specific impact of corticosteroid therapy, diagnostic strategies for distinguishing anemia of inflammation from IDA, and targeted therapeutic approaches, including biological agents.

Search Strategy

A literature search was conducted in PubMed (MEDLINE), Web of Science, Scopus, the Cochrane Library, and Google Scholar, restricted to peer-reviewed English-language articles. The following Medical Subject Headings (MeSH) terms and Boolean operators were applied: ("Rheumatoid Arthritis" [MeSH] AND "Anemia" [MeSH]) OR ("Iron Deficiency Anemia" [MeSH] AND "Arthritis, Rheumatoid" [MeSH]) OR ("Anemia of Chronic Disease" AND "Rheumatoid Arthritis") OR ("Hepcidin" AND "Rheumatoid Arthritis") OR ("Glucocorticoids" AND "Anemia" AND "Rheumatoid Arthritis") OR ("Tocilizumab" AND "Anemia" AND "Rheumatoid Arthritis") OR ("Soluble Transferrin Receptor" AND "Rheumatoid Arthritis"). Filters were applied to restrict results to randomized controlled trials (RCTs), cohort studies, and observational studies. Articles not available in English and those without accessible full text were also excluded. Reference lists of included articles were reviewed for additional eligible sources. Final selection prioritized high-quality evidence with direct relevance to the pathophysiology, diagnosis, corticosteroid effects, and treatment of anemia in RA.

Pathophysiology of anemia in RA

Anemia of inflammation; the central role of the hepcidin–ferroportin axis

Anemia of inflammation, sometimes referred to interchangeably as anemia of chronic disease (ACD), represents the most prevalent anemia type in RA and is mechanistically rooted in immune-mediated disturbances of iron homeostasis, erythropoiesis, and red cell survival (13,14). At the center of this pathophysiology stands hepcidin, a 25-amino acid peptide hormone synthesized predominantly in hepatocytes, which functions as the master regulator of systemic iron metabolism (15,16). Under conditions of systemic inflammation, activated immune cells release an array of proinflammatory cytokines, most importantly IL-6, which stimulates hepcidin transcription in hepatocytes via the JAK/STAT3 signaling pathway (16). The resulting hyperhepcidemia drives the degradation of ferroportin, the only known cellular iron export protein, on the surface of macrophages, duodenal enterocytes, and hepatocytes, thereby simultaneously reducing intestinal iron absorption and blocking the efflux of iron from tissue stores into the circulation (17). This process results in hypoferremia accompanied by paradoxically elevated or normal ferritin levels, the biochemical hallmark of anemia of inflammation (13). Ferritin, functioning as an intracellular iron storage protein, is additionally an acute-phase reactant whose transcription is directly upregulated by inflammatory mediators, causing it to rise independently of actual iron stores during active inflammation (18,19). The net consequence is iron sequestration within the reticuloendothelial system, with abundant iron locked in macrophages while developing erythroid progenitor cells in the bone marrow face functional iron starvation, a state termed iron-restricted erythropoiesis (20).

Cytokine-mediated suppression of erythropoiesis

Beyond the disturbances of iron homeostasis, inflammatory cytokines exert direct inhibitory effects on erythropoiesis at multiple levels. Erythropoietin (EPO), the primary erythropoietic hormone synthesized by peritubular cells of the kidney in response to tissue hypoxia, is inappropriately suppressed in the setting of anemia of inflammation (21). This blunted EPO response to anemia is a defining characteristic of anemia of inflammation and distinguishes it from other anemia etiologies in which EPO levels rise appropriately (22). A cohort study involving 330 RA patients demonstrated that anemic patients had significantly higher mean disease activity score (DAS28) scores (5.23 ± 1.42 versus 4.98 ± 1.35) and markedly elevated CRP levels (28.79 ± 12.56 mg/L versus 14.21 ± 8.35 mg/L) compared with non-anemic RA patients, providing direct clinical evidence linking the magnitude of systemic inflammation to the development and severity of anemia (9).

Concurrent iron deficiency in RA

While anemia of inflammation constitutes the dominant

anemia subtype in RA, true absolute iron deficiency contributes to anemia in approximately one/third of RA patients, either in isolation or superimposed upon anemia of inflammation (a condition designated ACD/IDA) (13,14). Patients with RA face several pathways to iron depletion that are distinct from the iron sequestration of anemia of inflammation. Long-term use of nonsteroidal anti-inflammatory drugs (NSAIDs), which is common in RA management, causes subclinical or overt gastrointestinal mucosal injury leading to occult or frank gastrointestinal blood loss, a significant source of iron depletion (23). Additionally, methotrexate and other conventional disease-modifying antirheumatic drugs (DMARDs) may affect gastrointestinal absorption and nutritional status over time, and chronic disease-related malnutrition or reduced dietary iron intake can further compound iron stores depletion (24). The distinction between ACD and IDA is of direct therapeutic relevance: patients with pure ACD benefit primarily from treatment of the underlying inflammatory disease and do not require iron supplementation, whereas those with true iron deficiency require specific evaluation for blood loss sources and targeted iron replacement therapy (25,26). The dietary inflammatory index (DII) has been evaluated as a measure of diet-related inflammatory potential and its association with anemia risk in RA; a large-scale population-based analysis using NHANES data (n = 2,287 RA patients) found that higher DII quartiles were significantly associated with increased anemia risk after full adjustment for confounders (Q4 vs. Q1: OR = 1.98), suggesting that pro-inflammatory dietary patterns may amplify the anemic burden in RA patients, with alcohol intake, iron, and zinc identified as the most influential dietary determinants (8).

Diagnostic challenges; distinguishing anemia of inflammation from IDA

Limitations of conventional iron parameters in the inflammatory setting

The accurate identification of iron depletion, whether absolute IDA or ACD with concurrent iron deficiency (ACD/IDA), in anemic RA patients is of fundamental clinical importance, yet it is diagnostically challenging because inflammation profoundly distorts conventional iron biomarkers (7). Serum ferritin, under non-inflammatory conditions, is the most reliable indicator of total body iron stores, with sensitivities of 63% to 100% and specificity of 92% to 98% for iron deficiency (27). This renders low ferritin thresholds insensitive, while elevated ferritin cannot be interpreted as evidence of adequate iron stores, creating a diagnostic paradox that undermines the clinical utility of ferritin-based assessments alone.

Transferrin saturation and red blood cell indices, mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH), are similarly affected by the inflammatory milieu. Transferrin synthesis is itself suppressed by inflammation and malnutrition, causing transferrin saturation to appear falsely normal or low, independent of actual iron status. Microcytosis and hypochromasia (reduced MCV and MCH), while characteristic of iron-deficient erythropoiesis, are late manifestations of iron depletion and show low sensitivity (23.8% for red blood cell indices alone in anemic RA patients) compared with other biomarkers (7).

The role of soluble transferrin receptor in inflammatory states

The soluble transferrin receptor (sTfR), a truncated extracellular fragment of the cell-surface transferrin receptor released into the circulation in proportion to cellular iron demand, has detected as a particularly valuable biomarker for iron deficiency diagnosis in the context of inflammation (28,29). A prospective cohort study of 116 consecutively enrolled anemic RA patients evaluated the diagnostic performance of sTfR measurement relative to standard parameters of iron status across the full range of inflammatory activity. In the total patient sample, sTfR demonstrated higher sensitivity (80.9%) for the detection of iron depletion (IDA or ACD/IDA) compared with combined standard parameters (66.7%), with comparable specificity and predictive values (7). Critically, this diagnostic advantage of sTfR was most pronounced in patients with high inflammatory activity (serum CRP above the median of 24.1 mg/L), in whom sTfR achieved 100% sensitivity and 100% negative predictive value for detecting iron depletion, compared with only 52.4% sensitivity for combined standard parameters. In contrast, in patients with lower inflammatory activity (CRP below the median), the combined use of conventional iron parameters yielded a higher sensitivity (76.2%) than sTfR alone (66.7%), suggesting that sTfR adds the greatest diagnostic value specifically in the highly inflamed, high-CRP subgroup of RA patients (7).

Mechanisms of glucocorticoid action in RA-related inflammation and hematopoiesis

Glucocorticoids (GCs) have been used for decades in the management of RA, exerting broad anti-inflammatory and immunosuppressive effects through multiple mechanisms; in the short term, these anti-inflammatory actions can be expected to reduce the cytokine-driven hepcidin response and potentially improve iron availability for erythropoiesis, which may modestly improve hemoglobin in patients with highly active, inflammation-dominant ACD (30). Corticosteroid use was documented in 40.84% of RA patients in a cross-sectional study, a finding that likely reflects the use of corticosteroids in patients with more severe and active disease rather than a direct anemia-inducing effect at low doses (31).

However, the long-term hematopoietic effects of cumulative GC exposure are considerably more complex. Clinical evidence demonstrates a paradoxical relationship

between high cumulative GC doses and systemic inflammation in patients with active RA; a prospective cohort study evaluating 72 long-treated RA patients (median disease duration 14 years) stratified by cumulative GC dose (cut-off 20 g) found that patients with active RA receiving high cumulative GC doses exhibited significantly elevated serum levels of 23 inflammation-related proteins compared with those receiving low cumulative doses; among the most prominently upregulated proteins were the chemokines CCL20, CCL3, and IL-8/CXCL8, the cytokines IL-17A, IL-17C, IL-18, oncostatin M, and the inflammatory mediators caspase-8, STAMBP, and 4E-BP1. Furthermore, in patients with active RA receiving high cumulative GC doses, significant derangements in blood cell count ratios were identified: elevated white blood cell counts, increased neutrophil-to-lymphocyte ratios and platelet-to-lymphocyte ratios, and decreased lymphocyte-to-monocyte ratios, compared with the low-dose group. These findings were not observed in patients with inactive RA, indicating that the elevated inflammatory milieu associated with high cumulative GC exposure is specific to contexts of persisting disease activity (32).

Inflammatory mechanisms linking disease activity to anemia severity

Cytokine profiles and their anemic consequences

The inflammatory cytokine milieu in active RA creates a self-reinforcing cycle of anemia perpetuation that is closely proportional to disease activity. Elevated circulating IL-6 acts simultaneously on multiple targets to drive anemia of inflammation; since, it stimulates hepcidin production in hepatocytes, promotes synthesis of acute-phase proteins including ferritin and CRP, suppresses albumin and transferrin synthesis, and inhibits EPO-responsive erythroid progenitor signalling (33,34). Besides, IL-6 decreases total iron-binding capacity and reduces hemoglobin levels while elevating the iron-regulatory hormone hepcidin, a mechanistic triad that consolidates its role as the central cytokine mediator of anemia of inflammation in RA (35). A population-based study found that anemic RA patients had significantly higher DII scores (a proxy for dietary and systemic pro-inflammatory burden) compared with non-anemic RA patients, further supporting the role of systemic inflammatory load in driving anemia (8).

Hepcidin as the molecular bridge between inflammation and anemia

Hepcidin has emerged as the molecular lynchpin connecting the systemic inflammatory response in infections and other inflammatory conditions to the hematopoietic consequences of anemia of inflammation, and its measurement has been explored as both a diagnostic and therapeutic target (36). Under conditions of high inflammatory activity, hepcidin concentrations are elevated compared with healthy controls, whereas patients with pure iron deficiency have low or undetectable hepcidin levels, and patients with ACD/IDA show intermediate hepcidin values in which the iron depletion signal partially overrides the inflammatory stimulus (37). This differential behavior of hepcidin across anemia subtypes has potential diagnostic utility: low hepcidin in an RA patient with anemia should prompt investigation for absolute iron deficiency, whereas elevated hepcidin in a moderately anemic RA patient point toward a dominant inflammatory etiology.

Treatment of anemia in RA; targeting inflammation

Tocilizumab and anti-IL-6 therapy

The most compelling evidence for treating anemia of inflammation by targeting its central inflammatory driver comes from studies of tocilizumab (TCZ), a humanized monoclonal antibody directed against the IL-6 receptor alpha subunit, which inhibits both classical (cis-) and trans-signaling cascades of IL-6 (38,39). By blocking IL-6R, TCZ interrupts the dominant stimulus for hepatic hepcidin induction via the JAK/STAT3 pathway, resulting in rapid and sustained reductions in circulating hepcidin concentrations (40). An analysis of a US healthcare database including 153,788 RA patients found that anemic patients treated with TCZ were 86% more likely to achieve a clinically meaningful hemoglobin increase of at least 1 g/dL at 2 years (OR 1.86; 95% CI 1.43–2.00) compared with patients receiving other treatments, including conventional DMARDs, other bDMARDs, or tofacitinib (41). Sarilumab, another anti-IL-6 receptor monoclonal antibody, demonstrated similar improving effects in RA clinical trials, further establishing the IL-6 blockade strategy as a targeted approach for improving RA (42,43).

TNF inhibitors and conventional DMARDs

TNF inhibitors are biologic disease-modifying antirheumatic drugs that selectively block tTNF-α, a key pro-inflammatory cytokine, thereby reducing pathologic inflammation in immune-mediated diseases such as RA (44). Remarkably, TNF inhibitors improve anemia in RA primarily by suppressing TNF-α–driven inflammation that impairs erythropoiesis and promotes ACD (45).

Iron supplementation and erythropoiesis-stimulating agents

Oral iron is generally reserved for mild iron deficiency in patients with low inflammatory activity, but its effectiveness is impaired in active RA because cytokine-driven hepcidin elevation reduces intestinal absorption and mobilization of iron stores; in patients with active inflammation, severe or symptomatic anemia, or intolerance to oral iron, intravenous iron (for example iron sucrose or ferric carboxymaltose) is preferred because it bypasses hepcidin-mediated absorption blockade and achieves faster, more reliable hemoglobin improvement (46).

The Mediterranean diet

The pathophysiological link between RA-associated inflammation and impaired iron homeostasis is well established through the hepcidin–IL-6 axis: inflammatory cytokines, particularly IL-6, directly stimulate hepatic production of hepcidin, an iron-regulatory hormone that induces ferroportin internalization and degradation, thereby sequestering iron within macrophages and enterocytes and restricting its availability for erythropoiesis (47). In a cross-sectional study by Nita et al, hepcidin demonstrated significant correlations with markers of anemia, iron metabolism, inflammation (IL-6, CRP and ESR), and erythropoiesis in RA patients, confirming its pivotal role at the intersection of inflammation-driven iron restriction and red cell health (48). Weiss et al further established that IL-6 and TNF-α upregulate hepcidin, leading to functional iron deficiency even in patients who appear iron-replete by conventional assays, a phenomenon distinctly prevalent in RA (49). The Mediterranean diet, characterized by high consumption of extra-virgin olive oil, fish, fruits, vegetables, legumes, and nuts, with low intake of red meat and saturated fats, has been proposed as a complementary dietary intervention to address both systemic inflammation and consequent iron restriction (50). In the landmark randomized controlled trial by Sköldstam et al, RA patients assigned to a Mediterranean diet for 12 weeks demonstrated a statistically significant reduction in DAS28 of 0.56, improved health assessment questionnaire (HAQ) scores, and enhanced vitality compared to a Western control diet, indicating a measurable anti-inflammatory dietary effect (51). Recently, McKellar et al in a prospective intervention involving 130 female RA patients, reported significant improvements in pain, early morning stiffness, patient global assessment, and HAQ scores at 3–6 months following a Mediterranean-type dietary intervention promoting fruits, vegetables, legumes, and monounsaturated fat substitution, along with a trend toward lower IL-6 levels in the intervention group (52). A cross-sectional Italian study by De Vito et al demonstrated that higher consumption of olive oil significantly reduced DAS28-CRP by ~0.70 and simplified disease activity index by ≥3.30 in RA patients with more severe or long-standing disease, attributing this benefit primarily to the polyphenolic compounds (oleuropein, oleocanthal, hydroxytyrosol) and monounsaturated fatty acids in olive oil, which modulate pro-inflammatory cytokine expression and inhibit metalloprotease activity at the synovial level (53). A systematic review and meta-analysis by Genel et al confirmed that a low-inflammatory/Mediterranean diet significantly reduced inflammatory biomarkers (CRP, IL-6) in RA patients with a standardized mean difference of −2.33 independently of weight change, reinforcing the notion that suppression of these cytokines through dietary modulation could secondarily alleviate hepcidin-mediated iron restriction (54). The green-Mediterranean diet variant, enriched with Mankai duckweed as a plant-based iron source alongside standard Mediterranean components, was demonstrated by Yaskolka Meir et al to produce a modest but significant increase in hemoglobin (0.23 g/dL, $P < 0.001$ versus control) over 6 months in overweight participants, further suggesting that a strategically structured Mediterranean diet can preserve or restore iron homeostasis (55). Collectively, the evidence supports a dual mechanism whereby the Mediterranean diet addresses iron deficiency in RA; since, first, by suppressing IL-6–mediated hepcidin induction through its anti-inflammatory phytochemicals and omega-3 fatty acids, thereby releasing the inflammatory block on intestinal iron absorption and macrophage iron release; and second, by directly enhancing dietary iron bioavailability through its high vitamin C content, reinforcing the rationale for the Mediterranean diet as an evidence-based adjunct nutritional strategy in the comprehensive management of RA-associated iron deficiency.

Conclusion

Anemia in RA is a multifactorial hematological complication with deep roots in the systemic inflammatory biology of the disease. The IL-6/hepcidin/ferroportin axis constitutes the dominant mechanistic pathway, with TNF-α, IFN-γ, and other cytokines contributing through direct EPO suppression, erythroid progenitor inhibition, and accelerated red cell destruction. True iron deficiency complicates anemia of inflammation in up to half of RA patients, and its recognition requires adoption of sTfR measurement, particularly in high-inflammatory states—alongside conventional iron parameters. Corticosteroid therapy presents a paradox: while acutely anti-inflammatory, high cumulative GC doses are associated with an amplified systemic inflammatory proteome and deranged blood count ratios in active RA, underscoring the need for GC minimization strategies. Anti-IL-6 receptor therapies, particularly TCZ, offer the most mechanism-aligned treatment for anemia of inflammation in RA, rapidly lowering hepcidin and restoring iron availability for erythropoiesis, while TNF inhibitors and conventional DMARDs contribute through broader disease activity suppression. Comprehensive anemia management in RA requires integrating inflammatory disease control, targeted iron supplementation where deficiency is confirmed, and individualized assessment of the hematopoietic side effects of both the disease and its treatments.

Conflicts of interest

The author declares that she has no competing interest.

Declaration of generative artificial intelligence (AI) and AI-assisted technologies in the writing process

During the preparation of this work, the author utilized AI (Perplexity and Grammarly) to refine grammar points and language style in writing. Subsequently, the author thoroughly reviewed and edited the content as necessary, assuming full responsibility for the publication's content.

Ethical issues

Ethical issues (including plagiarism, data fabrication, and double publication) have been completely observed by the author.

Funding/Support

None.

References

1. Ciofoaia EI, Pillarisetty A, Constantinescu F. Health disparities in rheumatoid arthritis. Ther Adv Musculoskelet Dis. 2022;14:1759720x221137127. doi: 10.1177/1759720x221137127.
2. Favalli EG. Understanding the Role of Interleukin-6 (IL-6) in the Joint and Beyond: A Comprehensive Review of IL-6 Inhibition for the Management of Rheumatoid Arthritis. Rheumatol Ther. 2020;7:473–516. doi: 10.1007/s40744-020-00219-2.
3. Nagib N, Nagib N, Gabra A, Schiller A, Emkey R. Case report: unusual and rare presentation of rheumatoid arthritis as multiple large synovial cysts in uncommon locations. Clin Med Insights Arthritis Musculoskelet Disord. 2025;18:11795441251379096. doi: 10.1177/11795441251379096.
4. Verma A, Patel P, Almalki WH, Sahebkar A, Kurmi BD, Kesharwani P. Recent Advances in Drug Delivery Approaches for Rheumatoid Arthritis. Curr Med Chem. 2025;32:396–415. doi: 10.2174/0929867331666230815112818.
5. Monaco F, Dimonte S, Jones SA. The role of IL-6 in rheumatoid arthritis comorbidity and implications for therapy. Biochim Biophys Acta Mol Cell Res. 2026;1873:120136. doi: 10.1016/j.bbamcr.2026.120136.
6. Sparks JA. Rheumatoid Arthritis. Ann Intern Med. 2019;170:Itc1–itc16. doi: 10.7326/aitc201901010.
7. Günther F, Straub RH, Hartung W, Fleck M, Ehrenstein B, Schminke L. Usefulness of Soluble Transferrin Receptor in the Diagnosis of Iron Deficiency Anemia in Rheumatoid Arthritis Patients in Clinical Practice. Int J Rheumatol. 2022;2022:7067262. doi: 10.1155/2022/7067262.
8. Song J, Zhang Y, Li A, Peng J, Zhou C, Cheng X, et al. Prevalence of anemia in patients with rheumatoid arthritis and its association with dietary inflammatory index: A population-based study from NHANES 1999 to 2018. Medicine (Baltimore). 2024;103:e38471. doi: 10.1097/md.0000000000038471.
9. Shah J, Farooq A, Zadran S, Kakar ZH, Zarrar M, Bhatti H. Prevalence of Anemia in Patients With Rheumatoid Arthritis Presenting at Multi-organization Tertiary Care Hospitals. Cureus. 2024;16:e72418. doi: 10.7759/cureus.72418.
10. Chen YF, Xu SQ, Xu YC, Li WJ, Chen KM, Cai J, et al. Inflammatory anemia may be an indicator for predicting disease activity and structural damage in Chinese patients with rheumatoid arthritis. Clin Rheumatol. 2020;39:1737–45. doi: 10.1007/s10067-019-04873-y.
11. Jindal A, Kaur K, Goel A, Setia P, Lanjewar S. Does Anemia Independently Influence the Erythrocyte Sedimentation Rate in Rheumatoid Arthritis? A Multivariate Analysis From North India. Cureus. 2026;18:e104704. doi: 10.7759/cureus.104704.
12. Sun Y, Liu J, Xin L, Wen J, Zhou Q, Chen X, et al. Factors influencing the Sharp score of 1057 patients with rheumatoid arthritis and anemia: a retrospective study. J Int Med Res. 2022;50:3000605221088560. doi: 10.1177/03000605221088560.
13. Lanser L, Weiss G. Anemia of Inflammation. Adv Exp Med Biol. 2025;1480:179–95. doi: 10.1007/978-3-031-92033-2_13.
14. Weiss G, Ganz T, Goodnough LT. Anemia of inflammation. Blood. 2019;133:40–50. doi: 10.1182/blood-2018-06-856500.
15. Rana S, Prabhakar N. Iron disorders and hepcidin. Clin Chim Acta. 2021;523:454–68. doi: 10.1016/j.cca.2021.10.032.
16. Liu J, Sun B, Yin H, Liu S. Hepcidin: A Promising Therapeutic Target for Iron Disorders: A Systematic Review. Medicine (Baltimore). 2016;95:e3150. doi: 10.1097/md.0000000000003150.
17. Afsar RE, Kanbay M, Ibis A, Afsar B. In-depth review: is hepcidin a marker for the heart and the kidney? Mol Cell Biochem. 2021;476:3365–81. doi: 10.1007/s11010-021-04168-4.
18. Baskaran A, Ramya V, Beeula A, Shamala S, Devi M, Sivakumar K. Estimation of Salivary Ferritin Levels in Subjects with Chronic Periodontitis with Type 2 Diabetes Mellitus. Indian J Dent Res. 2024;35:378–81. doi: 10.4103/ijdr.ijdr_211_24.
19. Qiu Z, Liu HH, Fan GZ, Chen WX, Hu P. The clinical implications of serum ferritin in Kawasaki disease: a helpful biomarker for evaluating therapeutic responsiveness, coronary artery involvement and the tendency of macrophage activation syndrome. Arch Med Sci. 2022;18:267–74. doi: 10.5114/aoms/144293.
20. Bennett LF, Liao C, Paulson RF. Stress Erythropoiesis Model Systems. Methods Mol Biol. 2018;1698:91–102. doi: 10.1007/978-1-4939-7428-3_5.
21. Urrutia AA, Afzal A, Nelson J, Davidoff O, Gross KW, Haase VH. Prolyl-4-hydroxylase 2 and 3 coregulate murine erythropoietin in brain pericytes. Blood. 2016;128:2550–60. doi: 10.1182/blood-2016-05-713545.
22. Sriram S, Xenocostas A, Lazo-Langner A. Erythropoietin in anemia of unknown etiology: A systematic review and meta-analysis. Hematology. 2016;21:234–40. doi: 10.1080/10245332.2015.1101972.
23. Kim TJ, Kim ER, Hong SN, Kim YH, Lee YC, Kim HS, et al. Effectiveness of acid suppressants and other mucoprotective agents in reducing the risk of occult gastrointestinal bleeding in nonsteroidal anti-inflammatory drug users. Sci Rep. 2019;9:11696. doi: 10.1038/s41598-019-48173-6.
24. Singh JA. Treatment Guidelines in Rheumatoid Arthritis. Rheum Dis Clin North Am. 2022;48:679–89. doi: 10.1016/j.rdc.2022.03.005.
25. Akpınar H, Çetiner M, Keshav S, Örmeci N, Törüner M. Diagnosis and treatment of iron deficiency anemia in patients with inflammatory bowel disease and gastrointestinal bleeding: iron deficiency anemia working group consensus report. Turk J Gastroenterol. 2017;28:81–7. doi: 10.5152/tjg.2017.17593.
26. Mi HC, Cui F, Du YT, Wang RT, Zhang R, Shi M. [Research progress on the regulation mechanisms of iron metabolism in anemia of chronic disease]. Sheng Li Xue Bao. 2022;74:639–47.
27. Garcia-Casal MN, Pasricha SR, Martinez RX, Lopez-Perez L, Peña-Rosas JP. Serum or plasma ferritin concentration as an index of iron deficiency and overload. Cochrane Database Syst Rev. 2021;5:Cd011817. doi: 10.1002/14651858.CD011817.pub2.
28. El-Gendy FM, El-Hawy MA, Rizk MS, El-Hefnawy SM, Mahmoud MZ. Value of Soluble Transferrin Receptors and sTfR/log Ferritin in the Diagnosis of Iron Deficiency Accompanied by Acute Infection. Indian J Hematol Blood Transfus. 2018;34:104–9. doi: 10.1007/s12288-017-0836-6.
29. Prenzel F, Kaiser T, Willenberg A, Vom Hove M, Flemming G, Fischer L, et al. Reference intervals and percentiles for soluble transferrin receptor and sTfR/log ferritin index in healthy children and adolescents. Clin Chem Lab Med. 2025;63:184–92. doi: 10.1515/cclm-2024-0369.
30. Berardicurti O, Ruscitti P, Pavlych V, Conforti A, Giacomelli R, Cipriani P. Glucocorticoids in rheumatoid arthritis: the silent companion in the therapeutic strategy. Expert Rev Clin Pharmacol. 2020;13:593–604. doi: 10.1080/17512433.2020.1772055.
31. Spivey CA, Griffith J, Kaplan C, Postlethwaite A, Ganguli A, Wang J. A Retrospective Analysis of Corticosteroid Utilization

Before Initiation of Biologic DMARDs Among Patients with Rheumatoid Arthritis in the United States. Rheumatol Ther. 2018;5:255–70. doi: 10.1007/s40744-017-0089-8.
32. Petrackova A, Horak P, Savara J, Skacelova M, Kriegova E. High cumulative glucocorticoid dose is associated with increased levels of inflammation-related mediators in active rheumatoid arthritis. Front Immunol. 2024;15:1505615. doi: 10.3389/fimmu.2024.1505615.
33. Victor M, Evgeniy H, Gergana T, Julia P, Vasil V, Borislav M, et al. Serum Hepcidin Levels in Multiple Myeloma. Clin Lab. 2017;63:1273–7. doi: 10.7754/Clin.Lab.2017.160637.
34. Țichil I, Mitre I, Zdrenghea MT, Bojan AS, Tomuleasa CI, Cenariu D. A Review of Key Regulators of Steady-State and Ineffective Erythropoiesis. J Clin Med. 2024;13. doi: 10.3390/jcm13092585.
35. Yacoub MF, Ferwiz HF, Said F. Effect of Interleukin and Hepcidin in Anemia of Chronic Diseases. Anemia. 2020;2020:3041738. doi: 10.1155/2020/3041738.
36. Wang CY, Babitt JL. Hepcidin regulation in the anemia of inflammation. Curr Opin Hematol. 2016;23:189–97. doi: 10.1097/moh.0000000000000236.
37. Ferrari F, Carini M, Zanella I, Treglia G, Luglio G, Bresciani R, et al. Potential Diagnostic Role of Hepcidin in Anemic Patients Affected by Inflammatory Bowel Disease: A Systematic Review. Diagnostics (Basel). 2024;14:375. doi: 10.3390/diagnostics14040375.
38. Biggioggero M, Crotti C, Becciolini A, Favalli EG. Tocilizumab in the treatment of rheumatoid arthritis: an evidence-based review and patient selection. Drug Des Devel Ther. 2019;13:57–70. doi: 10.2147/dddt.S150580.
39. Rubbert-Roth A, Furst DE, Nebesky JM, Jin A, Berber E. A Review of Recent Advances Using Tocilizumab in the Treatment of Rheumatic Diseases. Rheumatol Ther. 2018;5:21–42. doi: 10.1007/s40744-018-0102-x.
40. Merbl Y, Lopez Baltazar JM, Byron M, Chan SKC, Ehrlich JJ, Yu Q. Tocilizumab binds to canine IL-6 receptor and elicits in-vitro inhibitory biological response. Front Vet Sci. 2025;12:1645414. doi: 10.3389/fvets.2025.1645414.
41. Paul SK, Montvida O, Best JH, Gale S, Pethoe-Schramm A, Sarsour K. Effectiveness of biologic and non-biologic antirheumatic drugs on anaemia markers in 153,788 patients with rheumatoid arthritis: New evidence from real-world data. Semin Arthritis Rheum. 2018;47:478–84. doi: 10.1016/j.semarthrit.2017.08.001.
42. Raimondo MG, Biggioggero M, Crotti C, Becciolini A, Favalli EG. Profile of sarilumab and its potential in the treatment of rheumatoid arthritis. Drug Des Devel Ther. 2017;11:1593–603. doi: 10.2147/dddt.S100302.
43. Maioli G, Caporali R, Favalli EG. Lessons learned from the preclinical discovery and development of sarilumab for the treatment of rheumatoid arthritis. Expert Opin Drug Discov. 2022;17:799–813. doi: 10.1080/17460441.2022.2093852.
44. Lis K, Kuzawińska O, Bałkowiec-Iskra E. Tumor necrosis factor inhibitors - state of knowledge. Arch Med Sci. 2014;10:1175–85. doi: 10.5114/aoms.2014.47827.
45. Corrado A, Di Bello V, d'Onofrio F, Maruotti N, Cantatore FP. Anti-TNF-α effects on anemia in rheumatoid and psoriatic arthritis. Int J Immunopathol Pharmacol. 2017;30:302–7. doi: 10.1177/0394632017714695.
46. Chen WS, Liu CY, Lee HT, Tsai K, Lin YC, Tarng DC, et al. Effects of intravenous iron saccharate on improving severe anemia in rheumatoid arthritis patients. Clin Rheumatol. 2012;31:469–77. doi: 10.1007/s10067-011-1885-0.
47. Andrews NC. Anemia of inflammation: the cytokine-hepcidin link. J Clin Invest. 2004;113:1251–3. doi: 10.1172/jci21441.
48. Nita E, Bairaktari E, Kolios G, Migkos MP, Somarakis GP, Markatseli T, et al. Role of Hepcidin in Anemia of Chronic Disease in Rheumatoid Arthritis. J Lab Physicians. 2021;13:317–22. doi: 10.1055/s-0041-1732827.
49. Fraenkel PG. Anemia of Inflammation: A Review. Med Clin North Am. 2017;101:285–96. doi: 10.1016/j.mcna.2016.09.005.
50. Urquiaga I, Echeverría G, Dussaillant C, Rigotti A. [Origin, components and mechanisms of action of the Mediterranean diet]. Rev Med Chil. 2017;145:85–95. doi: 10.4067/s0034-98872017000100012.
51. Sköldstam L, Hagfors L, Johansson G. An experimental study of a Mediterranean diet intervention for patients with rheumatoid arthritis. Ann Rheum Dis. 2003;62:208–14. doi: 10.1136/ard.62.3.208.
52. McKellar G, Morrison E, McEntegart A, Hampson R, Tierney A, Mackle G, et al. A pilot study of a Mediterranean-type diet intervention in female patients with rheumatoid arthritis living in areas of social deprivation in Glasgow. Ann Rheum Dis. 2007;66:1239–43. doi: 10.1136/ard.2006.065151.
53. De Vito R, Fiori F, Ferraroni M, Cavalli S, Caporali R, Ingegnoli F, et al. Olive Oil and Nuts in Rheumatoid Arthritis Disease Activity. Nutrients. 2023;15:963. doi: 10.3390/nu15040963.
54. Genel F, Kale M, Pavlovic N, Flood VM, Naylor JM, Adie S. Health effects of a low-inflammatory diet in adults with arthritis: a systematic review and meta-analysis. J Nutr Sci. 2020;9:e37. doi: 10.1017/jns.2020.31.
55. Yaskolka Meir A, Tsaban G, Zelicha H, Rinott E, Kaplan A, Youngster I, et al. A Green-Mediterranean Diet, Supplemented with Mankai Duckweed, Preserves Iron-Homeostasis in Humans and Is Efficient in Reversal of Anemia in Rats. J Nutr. 2019;149:1004–11. doi: 10.1093/jn/nxy321.