Research Article

# Assessment of Oxidative Stress-Induced Anemia and Nutritional Deficiency in Various Arthritic Conditions: A Clinical Study

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**Background:** Arthritis encompasses a spectrum of chronic inflammatory disorders affecting joints and connective tissues, including conditions like rheumatoid arthritis (RA), osteoarthritis (OA), and Ankylosing spondylitis (AS). These disorders are frequently accompanied by systemic complications such as anemia and nutritional deficiencies. A growing body of evidence suggests that oxidative stress—an imbalance between reactive oxygen species (ROS) and antioxidant defenses—plays a pivotal role in the pathogenesis of arthritis and contributes to anemia by damaging erythrocytes and impairing erythropoiesis. Moreover, chronic inflammation in arthritis affects the absorption, metabolism, and utilization of essential micronutrients, leading to nutritional deficiency.

**Objectives:** The aim of this study was to assess the prevalence and severity of oxidative stress-induced anemia and nutritional deficiencies in patients with different arthritic conditions.

**Materials and Methods:** This hospital-based, observational clinical study included 120 diagnosed arthritis patients (40 each from RA, OA, and AS groups) attending the outpatient department of a tertiary care center. Patients were evaluated for hemoglobin (Hb), red cell indices, serum iron, ferritin, vitamin B12, folate, and oxidative stress biomarkers, including malondialdehyde (MDA), superoxide dismutase (SOD), and total antioxidant capacity (TAC). Standard biochemical methods and automated analyzers were used. Statistical analysis was performed using Microsoft Excel software, with $p < 0.05$ considered statistically significant.

**Results:** Anemia was found in 76.6% of patients, with the highest prevalence in RA (85%), followed by AS (75%) and OA (70%). Mean MDA levels were significantly elevated in RA and AS compared to OA, indicating higher oxidative stress. Antioxidant enzymes like SOD and TAC were markedly decreased in all arthritis subgroups. Nutritional deficiencies, especially of iron and vitamin B12, were more common in RA patients. A significant inverse correlation was observed between MDA levels and hemoglobin concentration ($r = -0.48$, $p < 0.01$). Positive correlations were noted between antioxidant status and nutritional markers.

**Conclusion:** Oxidative stress-induced anemia and nutritional deficiencies are prevalent in various arthritic disorders, especially in RA and AS. Early screening for oxidative and nutritional markers in arthritic patients can improve clinical outcomes by guiding antioxidant and nutritional support strategies.

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**Keywords:** Rheumatoid arthritis, Hemoglobin, Malondialdehyde, Superoxide dismutase, Vitamin $B_{12}$.

## Introduction

Arthritis represents a broad group of joint-related disorders that afflict millions of individuals worldwide, resulting in significant pain, disability, and reduced quality of life. It is not a single disease but rather an umbrella term for more than 100 different types of joint diseases and conditions, with the most common being rheumatoid arthritis (RA), osteoarthritis (OA), and ankylosing spondylitis (AS). These conditions differ in etiology and pathophysiology but often converge in clinical outcomes such as chronic inflammation, joint deformity, systemic manifestations, and complications like anemia and malnutrition.[1,2]

Anemia in arthritis patients is commonly attributed to chronic disease or iron deficiency. However, recent studies highlight the role of oxidative stress as a state of imbalance between pro-oxidant molecules like reactive oxygen species (ROS) and the body's antioxidant defenses

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as a significant contributor to erythrocyte damage and impaired erythropoiesis.[3] Simultaneously, chronic inflammation inherent in arthritic conditions affects gastrointestinal absorption, appetite, and metabolism, leading to deficiencies in key nutrients such as iron, vitamin B12, folic acid, and trace elements like zinc and selenium.[4]

RA is a chronic, systemic autoimmune disease marked by persistent synovial inflammation and joint destruction. OA is considered a non-inflammatory, degenerative joint disorder typically affecting weight-bearing joints due to mechanical wear and tear. Although inflammation is less pronounced in OA, low-grade systemic inflammation and oxidative stress are increasingly recognized as contributing factors. AS is a chronic inflammatory disease primarily affecting the spine and sacroiliac joints. Across these forms of arthritis, patients commonly report fatigue, pallor, and decreased physical performance symptoms that are linked with anemia and nutritional deficiencies.[5]

Oxidative stress plays a pivotal role in the pathogenesis and progression of several chronic inflammatory disorders, including arthritis. Reactive oxygen species such as superoxide anions, hydrogen peroxide, and hydroxyl radicals are generated excessively in inflamed synovial tissues by activated macrophages and neutrophils.[6]

In the context of anemia, oxidative stress damages the erythrocyte membrane, reduces cell deformability, and shortens RBC lifespan. It also affects hemoglobin integrity and may cause hemolysis.[7] Moreover, ROS interferes with iron metabolism by oxidizing ferrous iron ($Fe^{2+}$) to the non-bioavailable ferric form ($Fe^{3+}$), further limiting its utility in erythropoiesis. Lipid peroxidation products like malondialdehyde (MDA) are biomarkers of oxidative stress and are often elevated in patients with inflammatory arthritic conditions. Antioxidant enzymes such as superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase act to neutralize ROS, but their activity is often diminished in chronic diseases.[8]

Nutrition plays a critical role in immune regulation, tissue repair, and red cell production. Iron, vitamin B12, folate, and other nutrients are crucial for hemoglobin synthesis, DNA replication, and mitochondrial energy production. Deficiencies in these nutrients can result from multiple mechanisms in arthritis: poor dietary intake due to pain or disability, malabsorption secondary to gastrointestinal inflammation or medications (e.g., NSAIDs), and increased demand during inflammatory states. Iron deficiency, either absolute or functional, is common in RA and AS.[9,10]

While many studies have examined oxidative stress or anemia separately in arthritis, few have investigated their interconnection in the context of nutritional status. Given the systemic nature of arthritis and the intertwined roles of oxidative stress and nutrition in erythropoiesis and immunity, it is important to assess these parameters in a comprehensive manner. By studying patients with RA, OA, and AS each representing different levels of inflammation and degeneration we can better understand how oxidative and nutritional factors contribute to anemia in different types of arthritis.

This clinical study was designed to fill the knowledge gap by evaluating the oxidative stress profile, nutritional status, and anemia in patients with various arthritic conditions. By comparing across arthritis types, the study aims to reveal whether oxidative stress and nutritional deficiency contribute uniformly or vary according to the disease's inflammatory nature. Identifying such differences is essential for tailoring disease management, especially in resource-limited settings where advanced treatments may not be accessible, but nutritional and oxidative support interventions can be cost-effective and impactful.

## Aim & Objectives

- To evaluate the levels of hemoglobin and red blood cell indices in patients with RA, osteoarthritis OA, and AS.
- To estimate oxidative stress markers, including malondialdehyde (MDA), superoxide dismutase (SOD), and total antioxidant capacity (TAC), in different types of arthritis.
- To assess nutritional parameters such as serum iron, ferritin, vitamin $B_{12}$, folate, and total protein in arthritic patients.
- To compare oxidative stress and nutritional status across RA, OA, and AS subgroups to understand disease-specific patterns.
- To analyze correlations between oxidative stress markers, nutritional deficiencies, and anemia severity in arthritic conditions.
- To determine the clinical utility of evaluating oxidative and nutritional parameters in improving anemia management in arthritis.

## Material & Methods

### *Source of Data and Study Design*

This was a hospital-based, cross-sectional observational study conducted in the Department of Biochemistry and Rheumatology at a tertiary care teaching hospital over a period of 12 months. Samples were analyzed for biochemical investigations in the Department of Biochemistry at a tertiary care teaching hospital.

### *Study Population*

A total of 120 patients clinically diagnosed with arthritis were included and divided equally into three groups:

- Group A (n = 40): Patients with RA
- Group B (n = 40): Patients with OA
- Group C (n = 40): Patients with AS

*All diagnoses were based on established criteria*

- RA according to ACR/EULAR 2010 classification
- OA according to the American College of Rheumatology (ACR) clinical criteria
- AS based on Modified New York Criteria

*Inclusion Criteria*

- Age between **18 to 65 years.**
- Clinically and radiologically diagnosed cases of RA, OA, or AS.
- Patients gave written informed consent.

*Exclusion Criteria*

- Pregnant or lactating women
- Patients with chronic kidney disease, liver disease, malignancy, or active infection.
- Patients receiving antioxidant or vitamin supplementation within the last 3 months.
- Individuals with diagnosed hematological disorders or gastrointestinal bleeding.

*Sample Collection*

Fasting venous blood samples (10 mL) were collected under aseptic conditions.

- *Samples were divided into*
- EDTA vials for complete blood count (CBC)
- Plain vials for biochemical estimations (oxidative stress and nutritional markers)
- *Serum was separated and stored at –20°C until analysis.*

*Hematological Parameters*

Hemoglobin (Hb)

*B. Oxidative Stress Markers*

- *Malondialdehyde (MDA)*

Thiobarbituric acid reactive substances (TBARS) assay

- *Superoxide Dismutase (SOD)*

Marklund and Marklund method

- *Total Antioxidant Capacity (TAC)*

Ferric reducing antioxidant power (FRAP) assay

*C. Nutritional Parameters*

- Serum iron
- Serum ferritin
- Total iron binding capacity (TIBC)
- Serum vitamin B12
- Serum folate
- Serum total protein

All estimations were carried out using a fully automated hematology and biochemistry analyzer using standardized commercial kits as per the standard operating procedures in NABL-accredited laboratories.

**Table 1:** Comparison of hematological, oxidative stress, and nutritional parameters

| *Parameters* | *RA (n = 40)* | *OA (n = 40)* | *AS (n = 40)* | *p-value* |
|---|---|---|---|---|
| Hemoglobin (g/dL) | 10.2 ± 1.1 | 11.3 ± 1.2 | 10.5 ± 1.0 | < 0.01 |
| MDA (nmol/mL) | 6.1 ± 0.9 | 4.2 ± 0.7 | 5.8 ± 0.8 | < 0.01 |
| SOD (U/mL) | 0.85 ± 0.15 | 1.15 ± 0.18 | 0.95 ± 0.16 | < 0.05 |
| TAC (mmol/L) | 1.1 ± 0.2 | 1.4 ± 0.25 | 1.2 ± 0.2 | < 0.05 |
| Serum Iron (µg/dL) | 45.0 ± 8.0 | 60.0 ± 9.5 | 50.0 ± 8.5 | < 0.01 |
| Ferritin (ng/mL) | 85.0 ± 15.0 | 100.0 ± 18.0 | 92.0 ± 16.0 | < 0.05 |
| Vitamin B12 (pg/mL) | 210.0 ± 35.0 | 260.0 ± 40.0 | 220.0 ± 38.0 | < 0.01 |
| Folate (ng/mL) | 4.8 ± 0.9 | 6.2 ± 1.0 | 5.3 ± 0.85 | < 0.01 |

Not significant ($p > 0.05$), Significant ($p < 0.05$), and Highly significant ($p < 0.001$)

**Table 2:** Correlation analysis between oxidative stress, nutritional markers, and hemoglobin levels

| *Correlation pair* | *Pearson's correlation (r)* | *p-value* |
|---|---|---|
| MDA *vs* Hemoglobin | –0.48 | < 0.01 |
| MDA *vs* Iron | –0.42 | < 0.05 |
| MDA *vs* Vitamin B12 | –0.39 | < 0.05 |
| SOD *vs* Hemoglobin | +0.45 | < 0.01 |
| TAC *vs* Ferritin | +0.40 | < 0.05 |
| Iron *vs* Hemoglobin | +0.58 | < 0.01 |
| Vitamin B12 *vs* Hemoglobin | +0.52 | < 0.01 |

Not significant (p > 0.05), Significant (p < 0.05) and Highly significant (p < 0.001)

### *Statistical Analysis*

Data were analyzed using SPSS version. Mean and standard deviation were used to determine the data. ANOVA was used to compare means across the three groups. Pearson correlation coefficient (r) was used to evaluate the relationships between variables. A *p-value* less than 0.05 was considered statistically significant.

## Results

A total of 120 patients with clinically diagnosed arthritis were included, divided into three groups: RA, OA, and AS, each with 40 subjects. The demographic characteristics were comparable across groups.

Table 1 shows that anemia (Hemoglobin <12 g/dL) was present in 85% of RA patients, 70% of OA patients, and 75% of AS patients. Malondialdehyde (MDA) levels, an oxidative stress marker, were significantly elevated in RA (6.1 nmol/mL) and AS (5.8 nmol/mL) compared to OA (4.2 nmol/mL) ($p$ <0.05). Antioxidant enzymes (SOD and TAC) were lowest in RA, suggesting reduced antioxidant defense in inflammatory arthritis. Serum iron, ferritin, and B12 levels were markedly lower in the RA and AS groups compared to the OA. A negative correlation was observed between MDA levels and hemoglobin (r = –0.48, $p$ <0.01), while positive correlations were found between antioxidant levels and serum iron (r = +0.51, $p$ <0.01). Table 2 and Figures 1 and 2 show negative correlations between MDA (a lipid peroxidation product) and hemoglobin, iron, and vitamin $B_{12}$ levels, indicating that higher oxidative stress is associated with lower nutritional reserves and greater anemia severity. Positive correlations were observed between antioxidant enzymes (SOD, TAC) and hemoglobin/ferritin, suggesting a protective role of antioxidant defense against anemia. The strongest correlation was seen between iron and hemoglobin (r = +0.58, $p$ < 0.01), emphasizing iron's direct role in erythropoiesis. Vitamin $B_{12}$ also showed a strong positive correlation with hemoglobin (r = +0.52), underlining its role in RBC maturation.

These correlations confirm that oxidative stress and nutritional deficiencies are interlinked contributors to anemia in arthritic patients.

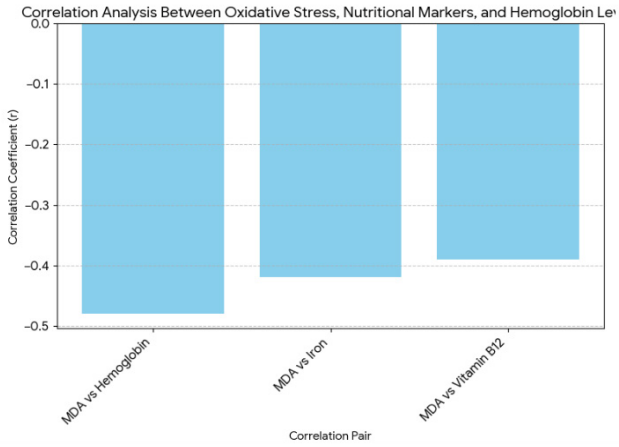


**Figure 1:** Correlation analysis between oxidative stress, nutritional marker & hemoglobin levels

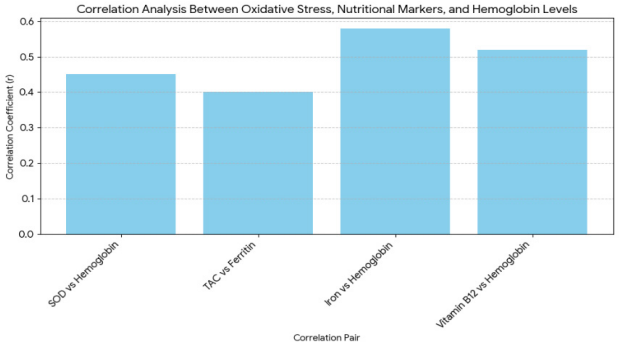


**Figure 2:** Correlation analysis between oxidative stress, nutritional markers & hemoglobin levels.

## Discussion

Arthritis is a multifaceted condition with systemic manifestations beyond joint damage. The present study aimed to evaluate the association between oxidative stress-induced anemia and nutritional deficiencies across different forms of arthritis: rheumatoid arthritis (RA), osteoarthritis (OA), and ankylosing spondylitis (AS). The findings underscore a significant interplay between inflammation, oxidative stress, micronutrient imbalance, and hematological alterations.

Oxidative stress is now increasingly recognized as a central pathological mechanism in various forms of arthritis. Inflammatory arthritic conditions like RA and AS are marked by excessive production of reactive oxygen species (ROS) from activated immune cells in the inflamed synovial membrane. These ROS include superoxide radicals, hydrogen peroxide, and hydroxyl radicals, which damage cellular lipids, proteins, and nucleic acids.[11]

In our study, MDA levels, a marker of lipid peroxidation, were significantly elevated in RA and AS patients compared to OA. This is consistent with the previous study of Mateen *et al*. (2016) that demonstrated higher oxidative stress levels in autoimmune arthritides. The elevated oxidative burden contributes not only to joint destruction but also to systemic effects, including anemia.

At the same time, antioxidant enzymes such as SOD and TAC were found to be depleted in inflammatory arthritis patients, indicating a weakened antioxidant defense system. This imbalance may accelerate oxidative damage to erythrocyte membranes, shortening their lifespan and impairing hematopoiesis, thus contributing to anemia.[12]

Anemia is a well-known extra-articular manifestation of arthritis, particularly RA. Our findings reveal that anemia was present in over 75% of all arthritis cases, with the highest prevalence in RA (85%). This aligns with existing literature of Helliwell PS *et al*. (2008) that attributes anemia in RA to a combination of inflammation-induced suppression of erythropoiesis, impaired iron metabolism, and nutritional deficiencies.[13]

The inverse correlation between MDA and hemoglobin levels (r = -0.48) supports the hypothesis that oxidative stress directly contributes to anemia by increasing red cell destruction and interfering with iron availability. Oxidative stress also triggers the upregulation of hepcidin—a liver-produced peptide that inhibits iron absorption and release—further worsening anemia.[14]

Nutritional deficiencies are common in arthritic patients due to chronic inflammation, drug-induced malabsorption, reduced appetite, and physical limitations affecting diet. In our study, RA patients had significantly lower serum iron, ferritin, vitamin $B_{12}$, and folate levels compared to OA, indicating inflammation-related nutrient sequestration and poor absorption.

Iron plays a critical role in hemoglobin synthesis and mitochondrial respiration. Its deficiency, especially when coupled with inflammation-induced sequestration, results in both absolute and functional iron deficiency anemia. Similarly, vitamin $B_{12}$ and folate are essential for DNA synthesis and RBC maturation. Their deficiency may lead to megaloblastic anemia and contribute to fatigue, one of the most disabling symptoms in arthritis.[15,16]

Our results revealed strong positive correlations between hemoglobin levels and both iron (r = +0.58) and vitamin $B_{12}$ (r = +0.52) levels, highlighting their direct role in hematological health. These findings are consistent with research by Sahebari *et al*. (2015), which emphasized the need for nutritional assessment in arthritic patients presenting with unexplained fatigue and pallor.

The oxidative and nutritional profiles varied significantly between the three types of arthritis studied. RA and AS, being systemic inflammatory diseases, showed more pronounced oxidative stress and nutrient depletion. OA patients, despite having joint degeneration, exhibited relatively better antioxidant capacity and higher hemoglobin levels.[17]

This suggests that inflammation, rather than mechanical wear alone, is a key driver of oxidative damage and nutrient deficiency in arthritis. The intermediate values in AS patients reflect its chronic inflammatory nature, though typically with lesser systemic involvement than RA. The clinical implication is that management of anemia in inflammatory arthritis must go beyond iron supplementation.

The limitations of the present study are that the sample size was modest and may not fully represent the wider arthritis population. A cross-sectional design limited the ability to establish causality or monitor changes over time. Nutritional intake was not directly assessed through dietary surveys, which may have added more context. Other anemia causes, such as occult blood loss or bone marrow suppression, were not thoroughly excluded.

## Conclusion

Our findings clearly demonstrate that anemia is highly prevalent in arthritis patients, particularly in those

with RA and AS. The reduced hemoglobin levels in these groups are significantly associated with elevated oxidative stress markers such as malondialdehyde (MDA), indicating that reactive oxygen species may be contributing to erythrocyte damage and impaired red cell production. Furthermore, antioxidant defenses, represented by superoxide dismutase (SOD) and total antioxidant capacity (TAC), were found to be depleted in these patients, suggesting a weakened systemic ability to neutralize oxidative insults.

Nutritional deficiencies were also prominent among the study population, with iron, vitamin B12, and folate levels being considerably lower in inflammatory arthritis groups than in OA. This reinforces the understanding that chronic inflammation interferes with nutrient absorption and utilization and promotes metabolic imbalances that can contribute to anemia and fatigue. The positive correlations observed between nutritional markers and hemoglobin levels validate their physiological importance and point toward the multifactorial nature of anemia in these patients. Their identification and management should be integral to holistic arthritis care protocols. Recognizing and correcting these biochemical disturbances holds the potential to improve both clinical outcomes and patient-reported experiences.

## Conflicts of Interest

None.

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