Abstract

Aging of the immune system results in increased inflammation, which enhances susceptibility to infectious diseases, infection-related complications of injuries, and the incidence of non-communicable diseases, including anemia. The prevalence of anemia in individuals over 65 years of age averages 12% of the community-dwelling population, 40% of hospitalized patients, and 47% of nursing home residents, with an overall prevalence of approximately 17% in the general elderly population. Inflammation induces a functional iron deficiency, characterized by decreased serum iron levels and reduced iron-binding capacity, despite normal or elevated ferritin concentrations. In functional iron deficiency, total body iron stores remain substantial, yet iron availability for erythropoiesis is restricted due to iron sequestration within macrophages and hepatocytes. Anemia of inflammation (AI), also referred to as anemia of chronic disease (ACD), represents a significant health concern in the geriatric population, correlating with diminished quality of life, increased hospitalization rates, and higher mortality. Understanding the underlying mechanisms of AI is critical for the development of novel diagnostic and therapeutic guidelines.

The objective of this study was to analyze the relationship between hematologic parameters and iron metabolism indices in individuals over 65 years of age with chronic inflammation and to evaluate the diagnostic utility of inflammatory markers in anemia detection. Additionally, a literature review was conducted to examine the epidemiology of anemia in the elderly, its etiological factors, clinical consequences, and the molecular mechanisms by which chronic inflammation initiates or sustains anemia progression.

The study included 113 individuals (mean age: 73.0 ± 7.2 years; women: n=62, men: n=51). Participants were allocated into two groups: anemic (AA, n=47, Hb <13 g/dL for women, Hb <14 g/dL for men) and non-anemic (NA, n=66, Hb ≥13 g/dL for women, Hb ≥14 g/dL for men). In the AA group, hematologic parameters such as RBC count, MCV, MCH, RDW, as well as serum iron and ferritin levels, were significantly lower compared to the NA group. Meanwhile, erythropoietin (EPO) and transferrin (Tf) concentrations remained within reference ranges but exhibited a trend toward higher values in the AA group. Across the entire study population, men demonstrated significantly lower serum iron and transferrin levels (84.38 ± 26.72 µg/dL and 2.75 ± 1.16 mg/dL, respectively) compared to women (100.82 ± 31.71 µg/dL and 3.17 ± 1.99 mg/dL, respectively), whereas ferritin concentrations did not differ between sexes.

Hepcidin (HPC) concentrations were 2.5-fold higher in the AA group than in the NA group. Additionally, HPC levels in men (16.79 ± 16.08 ng/mL) were more than twice as high as in women (7.00 ± 6.99 ng/mL), contributing to a further decline in serum iron levels among men. Similarly, elevated levels of pro-inflammatory cytokines IL-1β, IL-6, and TNFα were observed in the AA group. Hemoglobin concentration was negatively correlated with IL-1β (r_s = -0.581, $p < 0.0001$), suggesting impaired hemoglobin synthesis in the presence of inflammation. Receiver operating characteristic (ROC) curve analysis and odds ratio (OR) assessment for IL-1β demonstrated its high diagnostic value in age-related anemia (AUC=0.922, OR=72.374, 95% CI: 19.688–354.366). The concentration of peripheral blood mononuclear cells expressing CD34 and CD38 surface antigens was significantly higher in the AA group, indicating their role in compensatory mechanisms in anemia.

Based on conducted research and literature review, it has been showed that chronic inflammation is strongly associated with diminished systemic iron availability and anemia development in individuals over 65 years of age, with a higher risk observed in men compared to women. Simultaneous measurement of hepcidin and inflammatory mediators reveals their high diagnostic usefulness in differentiating anemic from non-anemic patients. The well-established link between chronic inflammation, impaired iron absorption in the gastrointestinal tract, and alterations in erythropoiesis supports the need for a diagnostic panel incorporating a spectrum of markers essential for the comprehensive evaluation of anemia in the elderly, with particular emphasis on hepcidin (HPC) and pro-inflammatory cytokines IL-1β and TNFα.