IRON DEFICIENCY ANAEMIA IN ACTIVE PULMONARY TUBERCULOSIS PATIENTS: UNDERSTANDING THE INTERPLAY AND IMPLICATIONS FOR MANAGEMENT

Rupak Bera*
Department of Medical Laboratory Technology, School of Allied Health Sciences, Swami Vivekananda University, Telinipara, Barasat-Barrackpore Rd, Bara Kanthalia, West Bengal - 700121, India.
Email: rupakbera164@gmail.com
DOI: https://doi.org/10.63001/tbs.2024.v19.i02.S1.pp30-32

KEYWORDS
Iron deficiency anemia
Pulmonary tuberculosis
Hepcidin
Ferritin
Inflammation

ABSTRACT
Iron deficiency anemia (IDA) is a common comorbidity in individuals with active pulmonary tuberculosis (PTB) and also it has negative impact on its treatment, yet its clinical significance and management remain underexplored. This article aims to elucidate the intricate relationship between iron status and pulmonary tuberculosis, examining its prevalence, etiology, and clinical implications. IDA in PTB patients can exacerbate symptoms such as fatigue and dyspnea, impairing quality of life and potentially hindering treatment outcomes. The underlying mechanisms linking IDA to PTB pathogenesis, including inflammation-induced hepcidin upregulation and altered iron metabolism, are discussed. Furthermore, challenges in diagnosing and managing IDA in PTB patients, including the limitations of traditional laboratory markers and concerns regarding iron supplementation, are addressed. Strategies for optimizing diagnostic approaches and tailoring iron supplementation regimes to mitigate potential adverse effects while ensuring treatment efficacy are proposed. Finally, the importance of a multidisciplinary approach involving collaboration between pulmonologists, hematologists, and infectious disease specialists in managing IDA in PTB patients is emphasized.

Enhancing our understanding of IDA in the context of PTB is crucial for improving clinical outcomes and reducing the burden of disease in this vulnerable population.

INTRODUCTION
Tuberculosis (TB) remains the leading cause of mortality attributable to a single pathogen [1]. Infection with Mycobacterium tuberculosis leads to a chronic pulmonary condition characterized by persistent granulomatous inflammation and significant lung tissue damage [2]. The global burden of TB continues to rise, with substantial morbidity and mortality rates [3]. In 2012, there were approximately 8.6 million new TB cases and an estimated 1.3 million TB-related deaths worldwide [4]. By 2016, TB affected around 10.4 million individuals and caused 1.7 million deaths globally [5]. Consequently, prevention of TB infection represents a critical global health priority. Many patients with active pulmonary TB present with reduced hemoglobin levels, which can directly impact TB-related morbidity. Anemia may arise from various causes, including iron deficiency and chronic inflammation. Anemia due to iron deficiency is associated with ferritin levels below 30 ng/mL, whereas anemia related to chronic disease is linked with ferritin levels exceeding 100 ng/mL [6]. Additionally, serum ferritin levels exceeding 100 ng/mL, whereas anemia related to chronic disease is linked with ferritin levels exceeding 100 ng/mL [6].

MECHANISM:
Anemia in tuberculosis (TB) is commonly attributed to nutritional deficiencies, malabsorption issues, and anemia of chronic disease (ACD) [15]. Inadequate dietary intake is a significant factor contributing to iron deficiency anemia (IDA). Reduced appetite, a typical symptom of TB, can lead to decreased food consumption, exacerbating the severity of IDA, especially when co-helminthic infections are present. Malabsorption disorders can also impair iron absorption, leading to IDA [16]. TB can involve the intestines either as a primary infection from ingested organisms or secondary to a pulmonary infection. Intestinal tuberculosis affecting the ileocecal region and presenting as ulcerative lesions is associated with malabsorption syndrome [17]. Tuberculosis (TB) infection is recognized for inducing systemic inflammation and lung pathology. Anemia of chronic disease, alternatively termed anaemia of inflammation (AI) or anemia of chronic illness (ACD), refers to a clinical condition characterized by the development of anemia in patients with infectious diseases (including fungal, bacterial, or viral infections like TB), inflammatory disorders, autoimmune conditions, or neoplastic diseases [18]. AI is attributed to inflammation-related mechanisms such as shortened red blood cell lifespan, impaired iron utilization by red blood cells, and reduced responsiveness to or production of erythropoietin [19].

Invasion by microorganisms triggers activation of T lymphocytes (CD3+), monocytes, and macrophages, initiating immunological responses that produce cytokines such as interferon-γ (IFN-γ) from activated monocytes and tumor necrosis factor-α (TNF-α), as well as interleukins (IL) such as IL-1, IL-6, and IL-10 from monocytes or macrophages. Lipopolysaccharides (LPS) are a key component of the outer membrane of gram-negative bacteria and act as potent stimulators of innate immunity [20]. Mycobacterium tuberculosis (MTB) controls inflammation, recognition, phagocytosis, replication in the phagosome, and cytosol escape during its intracellular life.
cycle, leading to regulated release of cytokines such as IL-1, TNF-α, IL-10, lipid mediators, and IFN-γ [21]. Anemia of chronic disease (ACD) is characterized by disturbances in iron homeostasis, with increased iron absorption and retention by reticuloendothelial system cells. Consequently, iron is sequestered from circulation and stored in the reticuloendothelial system, reducing iron availability for erythroid progenitor cells and leading to iron- 

Risk factors for anemia in adults with tuberculosis (TB) include low body mass index (BMI), HIV infection, helminthic coinfection, low selenium concentrations, older age, high retroviral load, elevated IL-6 concentrations, and female gender. In rat erythrocytes, dietary selenium significantly increased plasma glutathione peroxidase activity, leading to higher selenium levels in erythrocytes and improved resistance to oxidative stress. Glutathione peroxidase is an enzyme that helps defend against free radicals and oxidative stress [25].

Van Lettow et al. conducted a two-year study published in 2005 in the Zomba district, involving 500 individuals with pulmonary TB (PTB), including 370 HIV-positive and 130 HIV-negative participants. The study assessed erythropoietin (EPO), IL-6, plasma HIV load, micronutrient status, hemoglobin (Hb), retinol, tocopherol, carotenoids, ferritin, zinc, and selenium. IL-6 concentration was found to be 21.1 ng/ml in both HIV-positive and negative adults. Their findings indicated that low selenium levels, high HIV load, and IL-6 concentration are associated with an increased risk of anemia in TB patients [26].

Serum Ferritin
Ferritin is a blood protein that contains iron, and low serum ferritin levels indicate low iron storage and iron deficiency. Serum ferritin is not only a blood protein but also an acute phase reactant and inflammatory marker that can be elevated in various inflammatory conditions. The normal acceptable range for ferritin levels is between 30 and 300 ng/ml in males and between 10 and 200 ng/ml in females [27]. In patients with pulmonary tuberculosis (PTB), ferritin levels can increase significantly, ranging between 500 and 800 ng/dl [28]. Ferritin levels do not decrease significantly within one month of anti-tuberculosis treatment (ATT), but they decrease substantially after 60 days of ATT [29]. Generally, anemia associated with TB tends to resolve by the end of six months of ATT.

Serum Transferrin and TIBC
An increase in transferrin levels typically indicates that the body needs more iron. Total iron-binding capacity (TIBC) is an indirect measure of transferrin levels. Hypoferremia, or low serum iron levels, can occur due to iron sequestration within cells of the reticuloendothelial system, resulting in decreased transferrin saturation. Consequently, transferrin levels are often low or normal in cases of anemia of chronic disease (ACD) [30].

ESR and CRP
Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are diagnostic parameters commonly used to evaluate inflammation. They are elevated in both acute and chronic inflammatory conditions [31]. While ESR and CRP are sensitive indicators of inflammation, it’s important to note that they lack specificity, meaning that elevated levels can be seen in various inflammatory and non-inflammatory conditions alike.

Conclusion:
This review paper explores the significant association between tuberculosis (TB) and anemia, aiming to analyze the underlying processes contributing to anemia development and to identify effective therapeutic strategies to mitigate the morbidity of TB-associated anemia. Cytokines and inflammatory markers such as TNF-α, IFN-γ, hepcidin, and various interleukins (ILs) play roles in the pathogenesis of anemia in patients with chronic diseases. Anemia of chronic disease (ACD) can be diagnosed using parameters including hemoglobin (Hb) levels, transferrin, hepcidin, total iron-binding capacity (TIBC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and soluble transferrin receptor (sTfR). Anemia in TB patients typically falls within the mild-to-moderate range and often resolves after completion of anti-tuberculosis treatment (ATT) alone. Administering iron therapy during the active phase of TB is generally not recommended. Further studies are needed to elucidate the frequency and prevalence of anemia and to establish its unique characteristics associated with TB infection itself. Data on disease incidence in high-risk populations are essential for early detection and a better understanding of anemia in chronic infections like TB. A multidisciplinary approach encompassing routine follow-ups, regular screening practices, early diagnosis, and ensuring medication compliance, alongside treating the underlying cause, can significantly reduce the incidence of TB-associated anemia.

References:


