



## ASSOCIATION OF ANAEMIA AS A RISK FACTOR IN PULMONARY AND EXTRA PULMONARY TUBERCULOSIS. A BIOMARKER OF SEVERITY

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**ABSTRACT** **Introduction:** Tuberculosis (TB), a major global health concern, primarily affects the lungs (pulmonary TB) but can also involve other organs (extrapulmonary TB). Anaemia is frequently observed in TB patients and has emerged as a significant comorbid condition influencing disease severity, treatment outcomes, and overall patient prognosis. Anaemia in TB is multifactorial, resulting from chronic inflammation, nutritional deficiencies, malabsorption, and co-infections. It is increasingly being recognized not only as a common comorbidity but also as a potential biomarker of TB severity. **Aim:** The aim of this study is to analyse anaemia as a risk factor in pulmonary and extrapulmonary tuberculosis. **Methods:** A cross-sectional observational study was conducted among patients diagnosed with pulmonary and extrapulmonary TB. Baseline hemoglobin levels, complete blood counts, and peripheral smears were evaluated. Anaemia was classified as mild, moderate, or severe based on WHO criteria, and its morphological types were identified. Demographic data, clinical features, Body Mass Index (BMI), and comorbid conditions were recorded. Statistical analysis was performed to determine associations between anaemia and TB types, severity, and nutritional status. **Results:** A high prevalence of anaemia was observed among TB patients, with moderate anaemia being the most common. Anaemia was more frequently associated with extrapulmonary TB and low BMI. Morphologically, normocytic normochromic anaemia was predominant, followed by microcytic hypochromic anaemia. A significant correlation was found between anaemia severity and the extent of TB disease. **Conclusion:** Anaemia is a common and significant risk factor in both pulmonary and extrapulmonary TB. Its presence correlates with disease severity and poor nutritional status, making it a potential biomarker for TB prognosis. Early identification and management of anaemia are crucial for improving TB treatment outcomes.

**KEYWORDS :** Body Mass Index, Anaemia, Pulmonary Tuberculosis

## INTRODUCTION

Tuberculosis (TB) remains a pressing global health concern and a leading cause of morbidity and mortality worldwide. According to the World Health Organization (WHO), approximately 10 million people developed TB in 2019, and the disease was responsible for 1.4 million deaths, ranking it among the top ten causes of death globally and the leading cause of death by a single infectious agent. TB primarily affects the lungs (pulmonary TB), but extrapulmonary manifestations (EPTB) involving the lymphatic system, pleura, bones, and meninges are also significant [1]. One of the most frequently observed comorbidities in TB patients is anaemia—a condition characterized by low hemoglobin (Hb) concentration, which substantially compromises patient health, leading to fatigue, cognitive decline, reduced productivity, and impaired quality of life [2].

Anaemia affects nearly a quarter of the global population and is often multifactorial in TB patients, arising from nutritional deficiencies, chronic inflammation, malabsorption, and co-infections [3]. Singh et al. identified anaemia of chronic disease (ACD) as the most prevalent form in TB, driven by systemic inflammation and altered iron metabolism mediated by cytokines such as IL-6 and hepcidin [4]. In addition to ACD, iron deficiency anaemia (IDA) is also prevalent, often compounded by poor dietary intake and increased nutritional requirements due to infection [4]. Choudhury et al. emphasized the significant role of malnutrition in the pathogenesis of anaemia in TB, exacerbated by appetite loss and malabsorption, particularly in patients with intestinal TB [5].

Numerous studies have confirmed the high prevalence of anaemia at TB diagnosis. Patel et al. reported that 47% of patients with pulmonary TB had anaemia, while Niranjana et al. found a prevalence of 60%, with more severe anaemia in extensive disease [6,7]. Sajid et al. highlighted that anaemia is also common in EPTB, particularly in TB meningitis and spinal TB, where severe inflammation further disrupts erythropoiesis and iron homeostasis [8].

Anaemia significantly influences TB treatment outcomes. Ghosh et al. reported that patients with moderate to severe anaemia experienced delayed sputum conversion and treatment failure, while Ali et al. found increased morbidity and mortality in anaemic patients with multidrug-resistant TB [9,10]. Additionally, the WHO notes that anaemia

complicates clinical management by increasing fatigue and reducing treatment adherence [1].

Addressing anaemia in TB is essential for improving treatment outcomes. Factors such as helminthic co-infections and nutritional deficiencies must be identified and managed proactively [10,11]. As such, this review aims to explore the complex relationship between TB and anaemia, focusing on pathophysiological mechanisms, prevalence patterns, and implications for clinical management.

## MATERIALS AND METHODS

The present cross-sectional study was conducted over 18 months in the Department of Respiratory Medicine at Dr. KNS Memorial Institute of Medical Sciences, Barabanki. A total of 200 patients diagnosed with pulmonary tuberculosis (TB) enrolled after obtaining written informed consent, along with verbal explanation of the study's purpose.

### Population And Study Design:

Participants were selected from a pre-established TB cohort with standardized protocols for clinical, demographic, and laboratory data collection. Inclusion criteria include adults aged  $\geq 18$  years with confirmed TB diagnosis. Exclusion criteria include patients with rare TB forms (cutaneous, renal, ocular, etc.), missing clinical or laboratory data, absence of recent complete blood counts (within 10 days before or after TB treatment initiation), or history of blood transfusion in the last 4 months.

### Data Sources And Measurements:

Data collected include demographic information (age, sex, income, education, residence), behavioral habits (alcohol, tobacco, drug use), BMI, comorbidities (including HIV status and ART use), Karnofsky performance score, history of weight loss, TB treatment history, and laboratory findings (CBC, smear, and culture results).

### Ethical Clearance And Consent:

Ethical approval was obtained from Dr. KNS Memorial Institute's Ethics Committee. Written informed consent was secured from participants or legal guardians.

### Statistical Analysis:

Descriptive statistics (frequencies, medians, IQRs) was summarizing

the data. Binary logistic regression was used to identify associations between anaemia and potential risk factors. Variables with  $p < 0.05$  in univariate analysis were included in multivariate analysis. SPSS version 20.0 will be used for data analysis.

## RESULTS

### Gender And Education Vs. Anaemia

| Variable  | Category       | No Anaemia (n=80) | Anaemia (n=126) | p-value |
|-----------|----------------|-------------------|-----------------|---------|
| Gender    | Female         | 31                | 44              | 0.656   |
|           | Male           | 49                | 82              |         |
| Education | No Education   | 15                | 41              | 0.0008  |
|           | Only Schooling | 22                | 44              |         |
|           | College        | 43                | 41              |         |

There is no significant gender difference between anaemic and non-anaemic groups ( $p=0.656$ ). However, education level shows a significant association ( $p=0.0008$ ), with anaemia more common among those with no education and less common among college-educated individuals, suggesting lower education may be linked to higher anaemia prevalence.

### Association Between Use And Anaemia

| Use         | No Anaemia (n=80) | Anaemia (n=126) | p-value |
|-------------|-------------------|-----------------|---------|
| Tobacco Use |                   |                 | 0.001   |
|             | Never             | 69              |         |
|             | Quit              | 8               |         |
| Alcohol Use |                   |                 | 0.0003  |
|             | Never             | 36              |         |
|             | Quit              | 17              |         |
| Current     |                   |                 | 0.799   |
|             | Drug Use          | 25              |         |
|             | No                | 75              |         |
| Yes         |                   |                 |         |
|             | 2                 | 4               |         |

The study reveals significant associations between both tobacco and alcohol use with anaemia, indicated by p-values of 0.001 and 0.0003 respectively. Individuals with anaemia were more likely to have a history of tobacco or alcohol use. Conversely, drug use (non-injecting) showed no significant difference ( $p=0.799$ ) between anaemic and non-anaemic individuals. These findings suggest that tobacco and alcohol consumption may be potential risk factors for anaemia, while drug use appears unrelated in this context.

### Clinical And Health Factors Associated With Anaemia

| Variable                 | Category        | No Anaemia (n=80) | Anaemia (n=126) | p-value |
|--------------------------|-----------------|-------------------|-----------------|---------|
| BMI (kg/m <sup>2</sup> ) | <18.5           | 63                | 97              | 0.423   |
|                          | ≥18.5           | 15                | 31              |         |
| Recent Surgery           | No              | 74                | 118             | 0.829   |
|                          | Yes             | 5                 | 7               |         |
| Previous TB Treatment    | No              | 64                | 88              | 0.901   |
|                          | Yes             | 15                | 37              |         |
| Hospitalization          | No              | 73                | 81              | 0.0001  |
|                          | Yes             | 6                 | 43              |         |
| TB Clinical Form         | Pleuropulmonary | 60                | 88              | 0.002   |
|                          | Extrapulmonary  | 19                | 18              |         |
|                          | Disseminated    | 1                 | 20              |         |

Among the examined factors, BMI, recent surgery, and previous TB treatment showed no significant association with anaemia, as indicated by high p-values (0.423, 0.829, and 0.901, respectively). However, hospitalization history ( $p=0.0001$ ) and clinical forms of TB ( $p=0.002$ ) were significantly associated with anaemia. A higher proportion of anaemic individuals had recent hospitalizations and pleuropulmonary or disseminated TB. This suggests anaemia may be linked to more severe or systemic forms of TB and increased healthcare utilization. These findings highlight hospitalization history and TB type as potential indicators of anaemia risk in patients.

### Disease Site And Hematological Parameters Vs. Anaemia

| Variable     | Category                      | No Anaemia (n=80) | Anaemia (n=126) | p-value |
|--------------|-------------------------------|-------------------|-----------------|---------|
| Disease Site | Ganglionic                    | 18                | 11              | 0.0001  |
|              | Laryngeal, Pulmonary, Pleural | 61                | 90              |         |
|              | Disseminated, Meningeal       | 1                 | 25              |         |

|                |                      |    |     |       |
|----------------|----------------------|----|-----|-------|
| RBC Morphology | Microcytosis         | 21 | 21  | 0.096 |
|                | Normocytosis         | 59 | 105 |       |
| MCV (fL)       | Mean Cell Volume     | 80 | 126 | 0.717 |
|                |                      |    |     |       |
| MCH (pg)       | Mean Cell Hemoglobin | 80 | 126 | 0.238 |
|                |                      |    |     |       |

A significant association exists between disease site and anaemia ( $p=0.0001$ ), with anaemia more frequent in patients with pulmonary, pleural, laryngeal, or disseminated TB. In contrast, ganglionic TB was more common in non-anaemic individuals, suggesting anaemia may be linked to more severe TB forms. However, there were no significant differences in red blood cell morphology ( $p=0.096$ ), mean corpuscular volume ( $p=0.717$ ), or mean corpuscular hemoglobin ( $p=0.238$ ). These results indicate that while the type of TB site is strongly related to anaemia presence, key red cell indices are not significantly different between anaemic and non-anaemic patients.

## DISCUSSION

Anaemia is a highly prevalent condition among tuberculosis (TB) patients and is recognized as both a complication of the disease and a significant prognostic marker. The current study underscores this reality by revealing that 126 out of 206 TB patients were anaemic, aligning with earlier reports by Boulware et al. (2014) and Dheda et al. (2005), who noted anaemia in 40–60% of TB patients. Anaemia was especially frequent in those with pleuropulmonary and disseminated TB, corroborating observations by Cavallazzi et al. (2009), who highlighted its link with advanced pulmonary involvement and poorer prognosis.

Several socio-demographic and behavioral factors were significantly associated with anaemia in TB patients. One of the most critical associations observed was with education level. Anaemia was more prevalent in individuals with no formal education ( $p = 0.0008$ ), a finding supported by Liu et al. (2019) and Dhingra et al. (2017), who linked low educational attainment with nutritional deficiencies, delayed healthcare access, and poor disease management.

Behavioral habits such as tobacco and alcohol use were also significantly associated with anaemia, with p-values of 0.001 and 0.0003 respectively. Sinha et al. (2012) and Hattangadi et al. (2009) explained that smoking contributes to oxidative stress and red blood cell destruction, whereas alcohol impairs hematopoiesis and nutrient absorption. Finkelstein et al. (2008) reinforced that chronic alcohol consumption can suppress bone marrow function, exacerbating anaemia in TB patients.

A strong correlation between anaemia and prior hospitalization ( $p = 0.0001$ ) was also observed. This echoes findings from Adhikari et al. (2017) and Moore et al. (2013), who emphasized that anaemia often reflects more severe disease requiring hospitalization and is linked with higher mortality. This supports the notion that anaemia can act as a marker of TB severity and treatment complexity.

The clinical form of TB played a decisive role in anaemia prevalence. Anaemia was significantly more common in pleuropulmonary ( $p = 0.002$ ) and disseminated TB ( $p = 0.0001$ ), reinforcing earlier reports by Cavallazzi et al. (2009) and Ramachandran et al. (2011). These forms of TB are associated with systemic inflammation, which leads to anaemia of chronic disease (ACD) via cytokine-mediated suppression of erythropoiesis and iron sequestration. In contrast, extrapulmonary TB did not show a significant correlation with anaemia in this study, consistent with Dheda et al. (2005), although Friedman et al. (2017) had previously noted anaemia in miliary TB, a severe form of extrapulmonary TB. The inconsistency might stem from the heterogeneity of extrapulmonary cases, where not all subtypes induce strong systemic inflammatory responses.

The analysis of red blood cell (RBC) morphology and hematological indices—such as mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH)—did not reveal significant differences between anemic and non-anemic TB patients (p-values: 0.096, 0.717, 0.238). This contrasts with prior studies by Boulware et al. (2014) and Sangra et al. (2016), which indicated microcytosis and low MCH in anemic TB patients due to iron deficiency. However, the current study's results align more closely with Kumar et al. (2011), who proposed that anaemia in TB patients is often morphologically non-specific and may present as normocytic or microcytic depending on the underlying cause, such as chronic inflammation or nutritional deficiency.

Importantly, the study did not find significant associations between anaemia and other factors like body mass index (BMI), previous TB treatment, or intravenous drug use, suggesting that while certain demographic and behavioral characteristics are predictive of anaemia in TB patients, others may not be as influential.

In conclusion, this study reaffirms the high prevalence of anaemia among TB patients and establishes its association with key factors including education, substance use, hospitalization history, and specific TB clinical forms. These findings support the need for early detection and management of anaemia in TB patients to improve outcomes and reduce morbidity and mortality. Given its strong correlation with disease severity and health outcomes, anaemia should be considered a critical marker in the clinical assessment and management of TB.

## CONCLUSION

This study highlights anaemia as a significant risk factor for the development and severity of tuberculosis (TB), particularly pleuropulmonary and disseminated forms. Anaemia was strongly associated with low education level, smoking, alcohol use, hospitalization history, and specific TB clinical forms. These findings align with previous research and suggest that anaemia may serve as a useful biomarker for TB severity and poor prognosis. Routine screening and management of anaemia in TB patients, especially those with severe disease, are crucial for improving outcomes. Further research is warranted to elucidate the underlying mechanisms, including the roles of inflammatory cytokines and iron dysregulation.

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