Official Journal of Erciyes University Faculty of Medicine

DOI: 10.14744/cpr.2024.60895
J Clin Pract Res 2024;46(5):444–448

The Vicious Cycle of Malnutrition and Tuberculosis: A Narrative Review

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ABSTRACT

Tuberculosis (TB) represents a global health problem, affecting millions of individuals worldwide. A TB-related inflammatory response can occur, resulting in anorexia and increased catabolism, which may lead to malnutrition. Conversely, malnutrition is the most prevalent cause of secondary immunodeficiency and may contribute to both the incidence and prognosis of tuberculosis. In this context, there is a bidirectional relationship between malnutrition and TB. Nutritional interventions have the potential to significantly impact the prognosis of TB disease. This review aims to elucidate the relationship between malnutrition and TB and to highlight the efficacy of nutritional interventions in managing malnutrition in TB patients.

Keywords: Malnutrition, nutritional assessment, tuberculosis.

Cite this article as:
Ozer NT, Gundogan K. The Vicious Cycle of Malnutrition and Tuberculosis: A Narrative Review. J Clin Pract Res 2024;46(5):444–448.

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Submitted: 26.06.2024
Accepted: 10.07.2024
Available Online: 25.10.2024

Erciyes University Faculty of Medicine Publications - Available online at www.jcpres.com

INTRODUCTION

Tuberculosis (TB) is a chronic disease characterized by an infection with *Mycobacterium tuberculosis*, which is known to be one of the most lethal infectious organisms in the world. It is a significant public health concern, ranking as one of the thirteen causes of mortality worldwide.[1] The World Health Organization (WHO) has estimated that there were approximately 7.5 million new TB cases and 1.3 million deaths from TB in 2022.[2] The emergence of drug-resistant strains of TB, which are resistant to the two most powerful and effective TB drugs (rifampicin and isoniazid), represents a significant challenge to public health and TB control.[3] The development of TB is influenced by a number of risk factors, including an individual's previous exposure history, the environment in which they live, their smoking and alcohol consumption habits, the presence of tumors, and their nutritional status.[4]

Malnutrition represents the most prevalent cause of secondary immunodeficiency, affecting both innate and adaptive immunity. It is referred to as "nutritionally acquired immune deficiency syndrome." Malnutrition stimulates several immune mechanisms, making individuals susceptible to various infections.[5] Two principal mechanisms for the removal of pathogenic organisms from the body are phagocytosis and the complement cascade. In cases of undernutrition, both the opsonizing capacity of complement factor C3 and the ability of phagocytes to eliminate pathogens are significantly diminished.[6] Additionally, B-lymphocytes, macrophages, dendritic cells, and Kupffer cells are reduced in the presence of malnutrition. The mycobactericidal response, due to low zinc and copper levels, cell-based immunity, and cytokine secretion—which include tumor necrosis factor-alpha (TNF-α), interferon γ, and interleukin-12—are impaired.[7,8] Starvation-related malnutrition has been demonstrated to increase the incidence of TB by six to eight times.[9] Furthermore, a study reported that 34–88% of first-ever TB patients were at risk of malnutrition using different nutritional assessment tools.[10]

One indicator of malnutrition is the body mass index (BMI). A low BMI was found to be associated with the progression of latent TB infection to active TB disease.[8] A systematic review of 2.6 million patients with tuberculosis has demonstrated that the incidence of TB increases by 13.8% with each unit decrease in body mass index.[11] It has been posited that a normal BMI is protective against TB.[12] Moreover, a study demonstrated that obese and overweight elderly individuals exhibited a significantly lower incidence of TB compared to those with a normal BMI.[13]

However, malnutrition is both an etiological factor of TB and a clinical outcome of TB (Fig. 1). Malnutrition may result from reduced or insufficient dietary intake due to cytokine production, reduced absorption of nutrients, increased energy requirements, and increased loss, particularly urinary excretion of micronutrients, in infectious disease.[14] The severity of malnutrition in TB is influenced by the severity of the disease and, in particular, the inflammatory response, which results in catabolism and anorexia.[5]

It has been demonstrated that the presence of active TB increases the resting metabolic rate by approximately 14%.[15] Despite the increased energy requirements associated with TB, inadequate energy and protein intake can result in protein-energy malnutrition (PEM).[16] Furthermore, in TB, despite adequate energy intake, the restructuring of protein stores may be delayed due to the anabolic block, which is characterized by increased amino acid catabolism and turnover.[16] It has been demonstrated that increased circulating concentrations of interleukin-6 (IL-6), TNF-a, and other cytokines may cause weight loss, cachexia, and anorexia.[17]

Malnutrition can result in increased disease severity, delayed sputum conversion, malabsorption of anti-TB drugs, hepatotoxicity associated with TB drugs, decreased or delayed Bacillus Calmette-Guérin (BCG) vaccine response, disease relapse, and death.[4,18–20] Furthermore, the coexistence of multidrug therapy and rifampicin with malnutrition is associated with a higher incidence of adverse effects and increased mortality.[21]

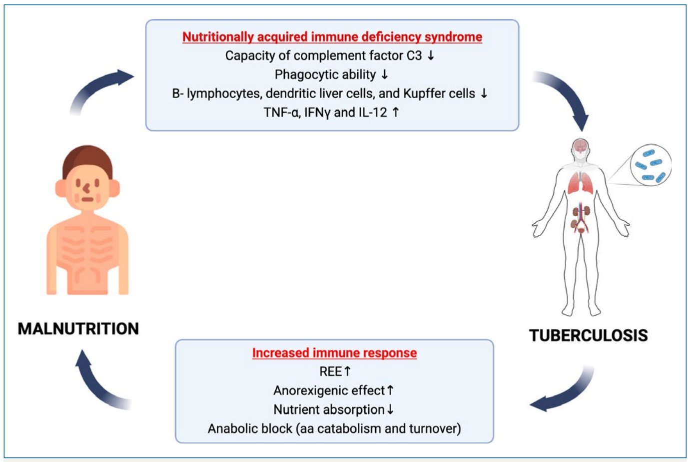

Figure 1. Mechanism of the vicious cycle between malnutrition and tuberculosis.

CLINICAL AND RESEARCH CONSEQUENCES

Malnutrition can be assessed using different tools such as anthropometric measurements, including BMI, mid-upper arm circumference, and screening or assessment tools with or without measurement of daily food intake.[22] A meta-analysis of 48 studies employing diverse nutritional assessment methodologies revealed that 48% of TB patients exhibited malnutrition.[23] The majority of studies have used BMI as the sole indicator for assessing nutritional status in TB patients.[24] Malnutrition is associated with reduced lean body mass.[25] In patients with a normal or high BMI but low lean mass, malnutrition may be overlooked if BMI assessment is used alone.

Hung et al.[26] performed a study investigating the nutritional status and dietary intake of 221 inpatients with pulmonary TB. It was reported that 85.5% of patients could not meet their daily energy requirements and approximately 90% of them did not receive sufficient dietary magnesium, calcium, zinc, and vitamin D. Furthermore, a study demonstrated that the severity of pulmonary TB was associated with reduced nutrient intake.[27]

THE MANAGEMENT OF MALNUTRITION IN TUBERCULOSIS

The assessment of nutritional status plays a crucial role in the prevention of malnutrition in vulnerable groups. Furthermore, it represents the initial stage of a possible nutritional intervention. In TB patients, it is recommended that screening and assessment for malnutrition be conducted at the time of diagnosis, as well as on a regular basis.[28] A malnutrition assessment tool, such as the Global Leadership Initiative on Malnutrition (GLIM),[29] can be employed to assess the condition. It is recommended that patients who are malnourished or at risk of malnutrition receive nutrition counseling and, if required, therapeutic and supplementary nutrition support such as food fortification, enteral nutrition, or parenteral nutrition.[28]

It is recommended that patients consume 30–35 kilocalories per kilogram of daily energy and at least 1 g/kg/day of protein.[28] In the event of insufficient energy intake, nutritional interventions can be employed as a means of providing the necessary sustenance. Nutritional interventions have the potential to yield significant outcomes, including increased body weight, improved handgrip strength, cure of TB, and reduced mortality.[30–32] Dietary habits, particularly those involving foods containing high-quality protein, can influence the prognosis of TB.[33]

Some studies have focused on the supplementation of micronutrients, including vitamins A, C, E, and D, as well as zinc, copper, selenium, and iron, in the context of secondary immunodeficiency.[34–39] It should be noted that these studies are subject to certain limitations, including the composition of the study population, the study design employed, and the quality of the research. At present, there is no reliable evidence on the effects of micronutrient supplementation.[28]

CONCLUSION

The vicious cycle of malnutrition and TB has been linked with possible effects on innate and adaptive immune responses. However, further investigation is required using modern immunological methods to achieve a deeper understanding of the impact of malnutrition on the TB prognosis, particularly with regard to sputum culture conversion, relapse, and mortality. Proper nutritional interventions can provide opportunities to reduce the occurrence of TB and improve clinical outcomes. It is important to provide individualized nutritional intervention after a comprehensive nutritional assessment in TB patients.

Author Contributions: Concept – NTO, KG; Design – NTO, KG; Supervision – NTO, KG; Resource – NTO, KG; Materials – NTO, KG; Data Collection and/or Processing – NTO, KG; Analysis and/or Interpretation – NTO, KG; Literature Search – NTO, KG; Writing – NTO, KG; Critical Reviews – NTO, KG.

Conflict of Interest: The authors have no conflict of interest to declare.

Use of AI for Writing Assistance: Not declared.

Financial Disclosure: The authors declared that this study has received no financial support.

Peer-review: Externally peer-reviewed.

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