Journal of Pharmaceutical and Sciences
Electronic ISSN: 2656-3088 DOI: https://doi.org/10.36490/journal-jps.com
Homepage: https://journal-jps.com
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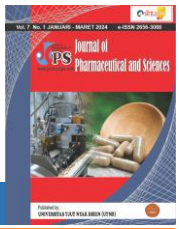
ORIGINAL ARTICLE JPS. 2025, 8(2), 960-966



Nutritional Status and Its Impact on Pulmonary Tuberculosis Recurrence at The Surakarta Public Pulmonary Health Center

Hubungan Status Gizi dan Kekambuhan Tuberkulosis di Balai Besar Kesehatan Paru Masyarakat Surakarta

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Abstract

Malnutrition can weaken the immune system, thereby increasing the risk of *Mycobacterium tuberculosis* infection. The aim of this study was to determine the risk of tuberculosis (TB) recurrence associated with the nutritional status of TB patients. This study was conducted at the Surakarta Center for Lung Health in 2017 using a case-control design. The study included 15 individuals in the control group (patients who had been cured of TB) and 15 individuals in the case group (patients who experienced TB recurrence). Inclusion criteria for this study were TB patients aged 18-65 years, both male and female, who had completed the full course of TB treatment, and who had complete data on nutritional status measured through Body Mass Index (BMI) and documented dietary intake in medical records. Patients with metabolic disorders or chronic diseases other than TB that could influence nutritional status were excluded. Data were collected from medical records and analyzed using SPSS version 25. The results showed that patients with poor nutritional status (below the normal BMI) had a significantly higher risk of TB recurrence ($p = 0.028$). Another finding indicated that patients who had a habit of consuming alcohol also had a higher likelihood of TB recurrence ($p = 0.001$). The conclusion of this study is that poor nutritional status plays a role in the occurrence of recurrent tuberculosis.

***Keywords*:** *Tuberculosis, Recurrence, Case-Control.*

Abstrak

Penurunan status gizi dapat melemahkan sistem kekebalan tubuh sehingga meningkatkan risiko infeksi *Mycobacterium tuberculosis*. Tujuan dari penelitian ini adalah untuk mengetahui risiko kekambuhan tuberkulosis (TB) yang dikaitkan dengan status gizi pasien TB. Penelitian ini dilakukan di Balai Besar Kesehatan Paru Masyarakat Surakarta pada tahun 2017 dengan rancangan penelitian case control. Terdapat 15 orang dalam kelompok kontrol (pasien TB yang sembuh) dan 15 orang pada kelompok kasus (pasien TB yang mengalami kekambuhan TB). Kriteria inklusi dalam penelitian ini adalah pasien TB berusia 18-65 tahun, baik laki-laki maupun perempuan, yang telah menyelesaikan pengobatan TB secara penuh, serta pasien yang memiliki data lengkap mengenai status gizi yang diukur melalui Indeks Massa Tubuh (IMT) dan asupan gizi yang tercatat dalam rekam medis. Pasien juga harus tidak memiliki gangguan metabolik atau penyakit kronis selain TB yang dapat mempengaruhi status gizi. Data diambil dari rekam medis dan diolah menggunakan SPSS versi 25. Hasil penelitian menunjukkan bahwa pasien dengan status gizi yang buruk (di bawah IMT normal) memiliki risiko lebih tinggi untuk mengalami kekambuhan tuberkulosis (p = 0,028). Temuan lain menunjukkan bahwa pasien yang memiliki kebiasaan mengonsumsi alkohol juga memiliki potensi kekambuhan TB yang lebih tinggi (p = 0,001). Kesimpulan dari penelitian ini adalah status gizi yang buruk berperan dalam terjadinya kekambuhan tuberkulosis.

Kata Kunci: *Tuberkulosis, Kekambuhan, Case-Control.*

Article History:
Received: 09/02/2025,
Revised: 10/05/2025,
Accepted: 10/05/2025,,
Available Online: 19/05/2025.
QR access this Article

https://doi.org/10.36490/journal-jps.com.792

Introduction

Tuberculosis (TB) remains one of the leading infectious diseases and a major global health challenge. According to the Global Tuberculosis Report 2023 by the World Health Organization (WHO), approximately 10.6 million people worldwide were diagnosed with TB in 2022, with an estimated 1.6 million deaths. [1] Indonesia ranks second in the world for TB cases, after India, with an incidence rate estimated at 969,000 cases per year. The high burden of TB in Indonesia underscores the need for a multidimensional approach to its prevention and control.

Malnutrition is one of the primary risk factors influencing the development and recurrence of TB. A decline in nutritional status can weaken the immune system, increasing the risk of Mycobacterium tuberculosis infection. Conversely, TB infection itself can lead to weight loss due to metabolic changes and inadequate nutrient intake [2]. This relationship suggests that nutritional status not only plays a role in TB incidence but also in the likelihood of recurrence.

Several studies have demonstrated that poor nutritional status, including protein-energy malnutrition and micronutrient deficiencies, increases the risk of active TB. For example, a study by Bhargava et al. (2020) in India found that malnutrition increases the risk of developing TB by two to three times. Similar findings have been reported in sub-Saharan Africa, where deficiencies in micronutrients such as zinc and vitamin D are associated with a higher incidence of TB [3].

TB recurrence is also a significant challenge in disease control. A study by Tiberi et al. (2019) found that patients with poor nutritional status have a higher risk of experiencing TB recurrence after completing treatment. This is due to the compromised immune system's inability to suppress latent infection. Nutritional interventions are therefore crucial in preventing recurrence and improving treatment outcomes. In Indonesia, a study by Dewi et al. [4] found that TB patients with poor nutritional status had a longer recovery time compared to those with good nutritional status. This study also highlighted the importance of integrating nutritional interventions into TB treatment programs. Additionally, research conducted in Surabaya concluded that vitamin D deficiency and iron-deficiency anemia are additional risk factors for TB recurrence [5].

Nutritional interventions have been proven effective in improving TB treatment outcomes. A meta-analysis by van Lettow et al. [3] demonstrated that high-energy and micronutrient supplementation during TB treatment can enhance recovery, reduce recurrence, and lower mortality rates. At the global level, WHO recommends nutritional support as part of a comprehensive approach for TB patients, particularly in high-prevalence countries.

Although many studies have highlighted the relationship between nutritional status and TB, data on TB recurrence in Indonesia remain limited. Therefore, further research is needed to explore the mechanisms underlying the impact of nutritional status on TB recurrence, particularly in populations with a high disease burden like Indonesia. These findings could help develop more effective nutrition-based interventions to reduce recurrence rates and improve the quality of life for TB patients.

Electronic ISSN : 2656-3088
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Experimental Section

This study employs a non-experimental design with a case-control approach to analyze the relationship between research variables and tuberculosis recurrence. The independent variables include gender, age, nutritional status, comorbidities, and smoking habits, while the dependent variable is tuberculosis recurrence. Research data were obtained from patient medical records at the Balai Besar Kesehatan Paru Masyarakat (BBKPM) Surakarta. The collected information includes demographic data (gender and age), nutritional status based on patient body weight, history of comorbidities, and smoking habits. Medical records were also used to identify patients who experienced tuberculosis recurrence.

The study population consists of patients who have undergone TB treatment at BBKPM Surakarta. The research sample includes 30 patients divided into two groups: 15 patients with recurrence (case group) and 15 patients without recurrence (control group). The sampling technique used is purposive sampling based on predetermined inclusion and exclusion criteria.

Data analysis was conducted to determine the relationship between independent variables and the dependent variable. The statistical test applied is the chi-square test or other appropriate tests for categorical data, with a significance level of 95% ($p < 0.05$).

The findings of this study are expected to provide insights into the factors contributing to tuberculosis recurrence, serving as a reference for efforts to prevent recurrence in TB patients in Indonesia.

Results and Discussion

Table 1. Baseline characteristic of the research subjects

Variables	Categories	
	Case (N=15)	Control (N=15)
Gender		
Male	11(73.3%)	9 (60%)
Female	4 (26.7%)	6 (40%)
Age		
Productive (<50 years)	8 (53.3%)	11 (73.3%)
Non-Productive (>50 years)	7 (46.7%)	4 (26.7%)

Men are more likely to contract tuberculosis (TB) than women, a trend observed worldwide. Several factors contribute to this disparity. Biological differences between the sexes may play a role, as hormonal and immune system variations can influence susceptibility to TB [6]. Additionally, men often have higher exposure to TB due to social and behavioral factors, such as increased likelihood of smoking and alcohol consumption, which are known risk factors for TB [7].

Regarding TB recurrence, men tend to experience higher rates compared to women. This can be attributed to several factors, including delayed healthcare-seeking behavior among men, which often results in more advanced disease at diagnosis and potentially incomplete treatment adherence [8]. Men are also more likely to have occupations that expose them to environments with a higher risk of TB transmission, such as mining, construction, or factory work, where prolonged exposure to overcrowded conditions or dust particles can increase the likelihood of reinfection [9].

Additionally, hormonal differences between men and women may influence TB recurrence rates. Testosterone, the predominant male sex hormone, has been shown to affect the immune system in ways that might make men more susceptible to infections like TB. Testosterone is known to suppress certain aspects of the immune response, particularly by reducing the function of T cells, which play a critical role in controlling Mycobacterium tuberculosis infections. This immune suppression may hinder the body's ability to mount an effective defense against the infection [10].

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In contrast, estrogen, the primary female sex hormone, has immune-enhancing properties. Estrogen has been shown to increase the production and activity of certain immune cells, such as T helper cells and macrophages, which are vital in the body's response to TB [11]. This could provide women with a slightly stronger immune response, helping them to control TB infections more effectively than men.

Furthermore, men's healthcare behaviors also play a role. Studies have found that men are less likely than women to seek healthcare early and may also have lower adherence to prescribed treatment regimens. These behavioral patterns could result from societal expectations surrounding masculinity, where men may avoid seeking medical help until symptoms are severe, leading to more severe or prolonged infections. Delayed diagnosis and incomplete treatment increase the risk of TB recurrence [12]

Occupational risks, combined with hormonal influences and healthcare-seeking behaviors, contribute to the higher incidence of TB recurrence among men. These factors suggest that addressing gender-specific health behaviors and occupational risks could improve TB prevention and treatment outcomes in men.

Tabel 2. Bivariate Analysis Result

Variable	Case (n=15)	Control (n=15)	P value	OR	95% CI
Nutritional Status					
Low	10 (66.7%)	1 (6.7%)	**0.001**	28	2.821 – 277.9
Normal	5 (33.3%)	14 (93.3%)			
Comorbidities					
Yes	2 (13.3%)	0 (0%)	0.143	-	
No	13 (86.7%)	15 (100%)			
Smoking Habit					
Yes	11 (73.3%)	6 (40%)	0.065	-	
No	4 (26.7%)	9 (60%)			
Habit of consuming alcohol					
Yes	11 (73.3%)	5 (33.3%)	**0.028**	5.55	1.146 – 26.412
No	4 (26.7%)	10 (66.7%)			

The results of bivariate tests on nutritional status on tuberculosis recurrence in this study, the following findings were obtained:

1. **Nutritional Status:** There was a significant difference in nutritional status between the case and control groups (p = 0.001). A total of 66.7% of the case group had low nutritional status, compared to only 6.7% in the control group. The Odds Ratio (OR) was 28 with a 95% Confidence Interval (CI) ranging from 2.821 to 277.9, indicating that individuals with low nutritional status were 28 times more likely to be in the case group than those with normal nutritional status.
2. **Comorbidities:** There was no significant difference in the presence of comorbidities between the case and control groups (p = 0.143). In the case group, 13.3% had comorbidities, whereas none of the control group did. Since the p value was greater than 0.05 and the OR was not calculated, this variable is not considered statistically significant.
3. **Smoking Habit:** There was a trend of difference in smoking habits between the two groups, but it did not reach statistical significance (p = 0.065). In the case group, 73.3% smoked, compared to 40% in the control group. Although the difference is noticeable, it is not strong enough to be considered statistically significant.
4. **Habit of Consuming Alcohol:** There was a significant association between alcohol consumption habits and the case group (p = 0.028). A total of 73.3% of the case group consumed alcohol, compared to 33.3% of the control group. The OR was 5.55 (95% CI: 1.146–26.412), indicating that individuals who consumed alcohol were 5.55 times more likely to be in the case group than those who did not.

Based on the results of the bivariate analysis, two factors were found to be significantly associated with the occurrence of cases:

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- Low nutritional status significantly increased the risk of being a case, with individuals having a 28 times higher risk compared to those with normal nutritional status.
- Alcohol consumption habits were also significantly associated, where individuals with this habit had a 5.55 times higher risk of being a case.

Meanwhile, comorbidities and smoking habits did not show a statistically significant association with the occurrence of cases in this study.

A study in Uganda found that malnourished individuals undergoing TB treatment had a higher likelihood of unsuccessful outcomes, including death and loss to follow-up [13]. Furthermore, malnutrition can alter the pharmacokinetics of anti-TB drugs. affecting their absorption and metabolism. This alteration may result in suboptimal drug concentrations, reducing treatment efficacy and increasing the risk of drug resistance. The World Health Organization emphasizes that malnutrition can influence how drugs are absorbed and processed, leading to treatment failure and potential toxicity [14] Malnutrition can alter the pharmacokinetics of anti-TB drugs, which include absorption, distribution, metabolism, and excretion of the drugs [15]. First, malnutrition can impair the gastrointestinal system by reducing gastric pH, bile secretion, and mucosal integrity, which in turn decreases the absorption of anti-TB drugs such as rifampicin, isoniazid, and pyrazinamide [16]. Second, malnutrition can reduce the body's protein stores, such as albumin, leading to an increase in the free drug concentration in the bloodstream, which increases the risk of drug toxicity [17]. Additionally, liver function can be compromised in malnourished individuals, reducing the activity of enzymes involved in drug metabolism, which may either slow down or accelerate the metabolism of anti-TB drugs [15]. Lastly, kidney function can be impaired by malnutrition, which decreases the glomerular filtration rate, leading to reduced drug excretion and increasing the risk of drug accumulation, potentially causing more severe side effects [16]. Therefore, patients with malnutrition require drug dose adjustments and more intensive nutritional support to achieve optimal therapeutic outcomes [17].

Addressing malnutrition is crucial for improving TB treatment outcomes. Integrating nutritional support into TB care can enhance immune function, ensure appropriate drug absorption, and reduce the risk of adverse treatment outcomes. A comprehensive approach that includes nutritional assessment and intervention is essential for the effective management of TB, particularly in populations with high rates of undernutrition.

Several comorbidities in tuberculosis patients lead patients to experience recurrence of tuberculosis. In this study, 13.3% of the population in the case group had type 2 diabetes mellitus. Diabetes mellitus (DM) significantly increases the risk of tuberculosis (TB) recurrence after successful treatment. A study by Lee et al. [18] found that the TB recurrence rate was higher in patients with DM compared to those without DM, particularly among men.

The compromised immune response in individuals with DM is a key factor contributing to TB recurrence. Chronic hyperglycemia impairs various immune functions, including the activity of macrophages and lymphocytes, which are essential for controlling TB infection. This immunosuppression makes it challenging to eradicate Mycobacterium tuberculosis completely, increasing the likelihood of relapse [19].

Additionally, DM can alter the pharmacokinetics of anti-TB medications, leading to suboptimal drug concentrations. This alteration may result in inadequate bacterial clearance during the initial treatment phase, leaving residual bacteria that can cause recurrence. A meta-analysis by Huangfu et al. [14] highlighted that individuals with diabetes mellitus (DM) have an increased risk of recurrent tuberculosis (TB). This risk is strongly associated with the immunosuppressive effects of chronic hyperglycemia, a common condition among people with DM. Hyperglycemia can impair the functions of macrophages, neutrophils, and T cells, all of which play critical roles in controlling *Mycobacterium tuberculosis* infection. As a result, individuals with DM are more susceptible to failing in eliminating the infection, both during the initial exposure and upon reactivation. Therefore, it is essential to develop tailored treatment strategies for this population, including strict blood glucose monitoring and an integrated approach to TB therapy and diabetes management. In Indonesia, this approach is supported through the collaborative policy between the National TB Control Program and the Non-Communicable Disease (NCD) Program, which encourages TB screening among DM patients and DM detection among TB patients, as outlined in the *National Guidelines for Tuberculosis Control* (2020) issued by the Ministry of Health of the Republic of Indonesia.

In this study 73.3% of the case group had a smoking habit. Smoking has been identified as a significant factor influencing the recurrence of pulmonary tuberculosis (TB). Research indicates that smoking can

Electronic ISSN : 2656-3088
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increase the risk of chronic lung diseases, including TB. The number of cigarettes smoked per day can exacerbate pulmonary TB infection and lead to failure in sputum conversion during the intensive phase of treatment [20].

The harmful substances in cigarette smoke, such as nicotine, tar, and carbon monoxide, can damage the respiratory system's defense mechanisms, particularly the mucociliary clearance. This impairment allows Mycobacterium tuberculosis to evade the body's immune responses, increasing the likelihood of reinfection and recurrence of TB [21]. Furthermore, smoking has been shown to elevate the risk of developing active TB. Studies have found that smokers have a 73% higher risk of TB infection and are more than twice as likely to develop active TB compared to non-smokers. The inhalation of cigarette smoke weakens the body's defense system, especially in the respiratory tract, making it more susceptible to TB bacteria.

Alcohol consumption has been identified as a significant risk factor for the recurrence of tuberculosis (TB). Recent studies have demonstrated that individuals who consume alcohol are at a higher risk of TB relapse and mortality compared to non-drinkers. Specifically, those consuming more than 40 grams of alcohol daily or diagnosed with alcohol use disorders exhibit an increased susceptibility to active TB. This heightened risk is attributed to both the social environments associated with alcohol consumption, which may facilitate TB transmission, and the detrimental effects of alcohol on the immune system

Excessive alcohol intake impairs the body's immune response, making individuals more susceptible to infections like TB. Alcohol can disrupt the function of macrophages and other immune cells, reducing the body's ability to contain Mycobacterium tuberculosis. This immunosuppression not only increases the risk of initial infection but also elevates the likelihood of disease reactivation and recurrence [22].

In this study, the results of the bivariate test between smoking habits and tuberculosis recurrence were significant (p=0.028). A person who has a habit of consuming alcohol is 5.55 times at risk of experiencing a recurrence of tuberculosis. Moreover, alcohol consumption has been linked to delays in TB diagnosis and treatment initiation. Individuals with heavy alcohol use may experience delays in seeking medical attention, leading to prolonged periods of infectiousness and increased transmission within communities. These delays can result in more severe disease progression and complications, further complicating treatment and increasing the risk of relapse [22].

Conclusions

Poor nutritional status affects the recurrence of tuberculosis patients. Making good nutrition one of the key factors for successful therapy in patients undergoing tuberculosis treatment.

Conflict of Interest

The Authors declare no conflict of interest regarding the publication of this article

Acknowledgment

The Authors would like to express their gratitude to Mitra Bunda Institute of Health for their support and to all individuals who contributed to this research.

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