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### Association of Metabolic Status and Hemoglobin Levels with Presumptive Tuberculosis Symptoms Among Indonesian Migrant Workers: A Cross-Sectional Study

Purnamawati Tjhin, Universitas Trisakti, Indonesia

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## Association of Metabolic Status and Hemoglobin Levels with Presumptive Tuberculosis Symptoms Among Indonesian Migrant Workers: A Cross-Sectional Study

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### ABSTRACT

Indonesian migrant workers face heightened vulnerability to tuberculosis (TB) due to crowded living conditions, occupational exposures, and restricted healthcare access. This study aimed to investigate the association between metabolic status (fasting blood glucose and total cholesterol) and hemoglobin levels with presumptive TB symptoms among Indonesian migrant workers residing in Johor Bahru, Malaysia. **Methods:** A cross-sectional study was conducted among 58 Indonesian migrant workers in Johor Bahru from April 2026. Presumptive TB was defined using an expanded symptom definition:  $\geq 1$  respiratory symptom (cough, productive cough, hemoptysis) OR  $\geq 2$  systemic symptoms (fever, night sweats, weight loss). Fasting blood glucose, total cholesterol, and hemoglobin were measured from capillary blood. Data analysis used Mann-Whitney U test and Fisher's exact test. **Results:** Among 58 participants (range 21-65 years, 67.2% female), 16 participants (27.6%) met the presumptive TB risk criteria. The most common symptoms were cough (19.0%) and night sweats (13.8%). Total cholesterol  $\geq 200$  mg/dL was associated with higher TB risk (OR=3.67, 95% CI: 1.03-13.07,  $p=0.044$ ). Hemoglobin and fasting glucose levels showed no significant association. **Conclusion:** Elevated total cholesterol is associated with heightened presumptive TB risk among Indonesian migrant workers. Metabolic screening, particularly lipid profiling, may enhance TB case detection in this vulnerable population.

## **INTRODUCTION**

Tuberculosis (TB) remains a leading cause of death from infectious diseases worldwide. The World Health Organization (WHO) Global Tuberculosis Report 2023 estimated 10.6 million new TB cases in 2022, with Southeast Asia accounting for nearly half of the global burden (World Health Organization, 2023). Malaysia, a major destination for Indonesian migrant workers, faces significant challenges in TB control, particularly among vulnerable populations (Mohidem et al., 2021).

Indonesian migrant workers (Pekerja Migran Indonesia/PMI) in Johor Bahru encounter multidimensional vulnerabilities to TB infection. Crowded living conditions, high-risk occupational exposures in construction and service sectors, and limited healthcare access contribute to disease transmission (Mohd Putera et al., 2023; Rast et al., 2025). Studies have documented higher infectious disease risks among migrant populations in Malaysia due to documentation issues, language barriers, fear of deportation, and financial constraints (Loganathan et al., 2020).

Beyond transmission risk factors, factors affecting treatment outcomes are also important to consider. A retrospective study in West Nusa Tenggara, Indonesia by Meiyanti et al. (2024) found that adequate treatment duration was a key factor for successful TB therapy, highlighting the importance of patient adherence to long-term treatment. This underscores the need for comprehensive support programs to ensure treatment adherence and improve outcomes. The emerging paradigm in TB epidemiology emphasizes host factors as important determinants of susceptibility to *Mycobacterium tuberculosis* infection. Metabolic status, including blood glucose and lipid profiles, is increasingly recognized as a critical factor in TB pathogenesis (Saxena et al., 2021). Diabetes mellitus has been consistently identified as a significant risk factor for active TB, with meta-analyses showing that type 2 diabetes patients have 4.11 times greater risk for drug-resistant TB (Irawan et al., 2025) and 1.9 times higher risk for active TB (Franco et al., 2024).

Disruptions in lipid metabolism may also influence TB pathogenesis. *Mycobacterium tuberculosis* can use host lipids, including cholesterol, to support intracellular survival and replication (Moopanar et al., 2023). In addition, TB has been associated with altered phospholipid, glyceride, and sphingolipid profiles that tend to normalize with treatment (Chen et al., 2021). Brake et al. (2025) further reported that dyslipidemia is linked to disease severity and inflammatory markers in TB patients. Hemoglobin may provide an indirect marker of TB severity: anemia is common in TB and may result from inflammation-driven hepcidin production with iron sequestration, malnutrition, and/or blood loss (Abaynew et al., 2023; Al-Bari., 2024).

However, comprehensive studies integrating metabolic parameters with TB symptoms among migrant worker populations remain limited. This study aimed to analyze the association between metabolic status (fasting blood glucose, total cholesterol) and hemoglobin levels with presumptive TB symptoms among Indonesian migrant workers in Johor Bahru, Malaysia, using an expanded risk definition that captures both respiratory and systemic symptoms.

## **LITERATURE REVIEW**

Tuberculosis (TB) remains a major global public health concern, with an estimated 10.6 million new cases reported worldwide in 2022, particularly concentrated in Southeast Asia (World Health Organization, 2023) . Migrant populations, including Indonesian migrant workers in Malaysia, are disproportionately affected due to structural and social vulnerabilities such as overcrowded living conditions, occupational exposure, and limited access to healthcare services (Loganathan et al., 2020; Mohd Putera et al., 2023; Rast et al., 2025) . These conditions increase both transmission risk and barriers to early diagnosis and treatment.

### **TB Risk Among Migrant Populations**

Previous studies have consistently demonstrated higher TB prevalence among migrant populations. A systematic review by Chen et al. (2025) reported a TB prevalence of 214.52 per 100,000 among migrants, with even higher rates among refugees and asylum seekers . Healthcare access barriers – such as legal status, language differences, and fear of deportation – further exacerbate disease burden in this group (Loganathan et al., 2020) . These findings highlight the need for targeted screening and prevention strategies in migrant worker populations.

### **Metabolic Factors and Tuberculosis**

Recent advances in TB epidemiology emphasize the role of host metabolic factors in disease susceptibility. Diabetes mellitus has been widely recognized as a significant risk factor for TB. A Cochrane systematic review by Franco et al. (2024) found that individuals with diabetes have approximately 1.9 times higher risk of developing active TB. Furthermore, Irawan et al. (2025) reported that type 2 diabetes increases the risk of multidrug-resistant TB by more than fourfold.

Mechanistically, hyperglycemia impairs immune function through multiple pathways, including macrophage dysfunction, reduced cytokine production, and impaired granuloma formation, ultimately increasing susceptibility to *Mycobacterium tuberculosis* infection (Al-Bari et al., 2024) . These findings support the concept of bidirectional screening for TB and diabetes, especially in high-risk populations (Boadu et al., 2024).

### **Lipid Metabolism and TB Pathogenesis**

Beyond glucose metabolism, lipid metabolism – particularly cholesterol – has emerged as an important factor in TB pathogenesis. *Mycobacterium tuberculosis* utilizes host lipids, including cholesterol, to support intracellular survival and replication within macrophages (Moopanar et al., 2023) . Alterations in lipid profiles, including phospholipids, glycerides, and sphingolipids, have been observed in TB patients and tend to normalize with successful treatment (Chen et al., 2021) .

Additionally, dyslipidemia has been associated with TB disease severity and inflammatory responses. Brake et al. (2025) demonstrated that abnormal lipid profiles persist even after treatment and correlate with systemic

inflammation. The concept of “metabolic scarring” proposed by Kagemann et al. (2025) further suggests a bidirectional relationship between TB infection and metabolic disorders, reinforcing the importance of metabolic health in TB progression

## **METHODS**

This observational analytical study employed a cross-sectional design. Data were collected at Sekolah Indonesia Johor Bahru (SIJB), Malaysia, during April 2026. This venue was selected as it serves as a gathering place for the Indonesian migrant community and offered convenient access to the target population. The site was selected in collaboration with the Consulate General of the Republic of Indonesia (KJRI) Johor Bahru. The target population was Indonesian migrant workers in Johor Bahru. Inclusion criteria were: (1) Indonesian citizens working in Johor Bahru; (2) age 18–60 years; (3) working in Malaysia for  $\geq 6$  months; and (4) providing written informed consent. Exclusion criteria were: (1) currently receiving TB treatment; (2) pregnant or breastfeeding; (3) use of medications that may affect metabolic parameters (corticosteroids, antidiabetics, statins, or iron supplements) within the past 3 months; and (4) severe chronic disease. Using purposive sampling with a snowball approach, 58 participants were included after excluding records with incomplete data. Fasting blood glucose (mg/dL) and hemoglobin (g/dL) were measured from capillary blood using the Easy-touch® GcHb monitoring system after a 10-hour fast, and total cholesterol (mg/dL) was measured using Autocheck® Total Cholesterol. Presumptive TB risk was defined using an expanded symptom-based criterion:  $\geq 1$  respiratory symptom (cough in the past 3 months, productive cough for  $> 2$  weeks, or hemoptysis) or  $\geq 2$  systemic symptoms (fever for  $> 1$  month, night sweats, or unintentional weight loss). This definition was used to increase sensitivity for detecting presumptive TB in migrant populations where symptoms may be underreported.

Demographic information including age, gender, educational background, occupation, and duration of employment was obtained through structured questionnaire administration. Physical examination included body weight and height measurements. Capillary blood samples were collected after a 10-hour fasting period. Participants reported their symptomatology during an interview-based assessment. All procedures were performed by trained personnel using calibrated equipment. Data were analyzed using SPSS version 26.0 (Normality was assessed using Shapiro-Wilk test. Due to non-normal distribution, median (minimum-maximum) and Mann-Whitney U test were used for numerical variables. Categorical variables were analyzed using Fisher's exact. Statistical significance was set at  $p < 0.05$ ).

This study was approved by the Ethics Committee of the Faculty of Medicine no 010/KER/FK/03/2026. All participants provided written informed

## **RESULTS**

A total of 58 Indonesian migrant workers were included in the final analysis after excluding nine incomplete records from the original 67 participants. The range age was 21–65 year, with the mean BMI 26.1 kg/m<sup>2</sup>. Using the expanded

definition ( $\geq 1$  respiratory symptom or  $\geq 2$  systemic symptoms), 16 participants (27.6%) met the presumptive TB risk criteria. Respiratory symptoms included cough in the past 3 months (19.0%), productive cough for  $>2$  weeks (5.2%), and hemoptysis (0%). Systemic symptoms included fever for  $>1$  month (5.2%), night sweats (13.8%), and unintentional weight loss (1.7%). Based on the risk classification, 12 participants (20.7%) met the criteria via respiratory symptoms only, 4 participants (6.9%) via systemic symptoms only ( $\geq 2$ ), and none met both criteria.

Table 1. Sociodemographic Characteristics of Participants (n=58)

| Characteristic                   | n  | %    |
|----------------------------------|----|------|
| Gender                           |    |      |
| Male                             | 19 | 32.8 |
| Female                           | 39 | 67.2 |
| Age group (years)                |    |      |
| 20-30                            | 7  | 12.1 |
| 31-40                            | 21 | 36.2 |
| 41-50                            | 21 | 36.2 |
| 51-60                            | 8  | 13.8 |
| $>60$                            | 1  | 1.7  |
| Education level                  |    |      |
| Incomplete elementary            | 2  | 3.4  |
| Elementary graduate              | 6  | 10.3 |
| Junior high school graduate      | 8  | 13.8 |
| Senior high school graduate      | 14 | 24.1 |
| University graduate              | 28 | 48.3 |
| Occupation                       |    |      |
| Education sector                 | 13 | 22.4 |
| Restaurant/F&B                   | 9  | 15.5 |
| Construction                     | 8  | 13.8 |
| Household worker                 | 6  | 10.3 |
| Cleaning services                | 6  | 10.3 |
| Others                           | 16 | 27.6 |
| Length of employment in Malaysia |    |      |
| $<1$ year                        | 4  | 6.9  |
| 1-5 years                        | 11 | 19.0 |
| 5-10 years                       | 14 | 24.1 |
| $>10$ years                      | 29 | 50.0 |

Individuals classified as having presumptive TB risk exhibited notably higher median total cholesterol levels (207.5 mg/dL) compared to those without such risk (191.0 mg/dL), reaching statistical significance ( $p=0.047$ ). Similarly, fasting blood glucose concentrations were elevated in the presumptive TB group (median 104.0 mg/dL) relative to the non-risk group (99.5 mg/dL), with statistical significance attained ( $p=0.035$ ).

Stratified by cholesterol thresholds, individuals with total cholesterol  $\geq 200$  mg/dL demonstrated substantially increased odds of meeting presumptive TB criteria (OR=3.67, 95% CI: 1.03-13.07,  $p=0.044$ ). This suggests that persons with

elevated cholesterol carry approximately 3.67-fold greater likelihood of fulfilling presumptive TB definitions. Elevated fasting blood glucose (>100 mg/dL) showed an association with presumptive TB risk (OR=2.22, 95% CI: 0.68-7.26), though this did not reach statistical significance ( $p=0.247$ ). Hemoglobin concentrations demonstrated no significant association with presumptive TB status. The median hemoglobin in the presumptive TB group was 14.2 g/dL versus 14.5 g/dL in those without risk ( $p=0.710$ ), indicating comparable oxygen-carrying capacity between groups. This finding suggests that overt anemia was not characteristic of this population, possibly reflecting early-stage disease manifestations or adequate nutritional status.(Table 2)

Table 2. Association between Metabolic Categories and Presumptive TB Risk

| Parameter             | Category   | TB Risk<br>(n=16) | No Risk<br>(n=42) | OR (95% CI)      | p-value* |
|-----------------------|------------|-------------------|-------------------|------------------|----------|
| Fasting blood glucose | >100 mg/dL | 10<br>(62.5%)     | 18<br>(42.9%)     | 2.22 (0.68-7.26) | 0.247    |
|                       | ≤100 mg/dL | 6<br>(37.5%)      | 24<br>(57.1%)     | Reference        |          |
| Total cholesterol     | ≥200 mg/dL | 11<br>(68.8%)     | 16<br>(38.1%)     | 3.67(1.03-13.07) | 0.044*   |
|                       | <200 mg/dL | 5<br>(31.3%)      | 26<br>(61.9%)     | Reference        |          |
| Hemoglobin            | Low**      | 2<br>(12.5%)      | 9 (21.4%)         | 0.52 (0.10-2.80) | 0.710    |
|                       | Normal     | 14<br>(87.5%)     | 33<br>(78.6%)     | Reference        |          |

\* $p<0.05$  Fisher's exact test \*\* Low hemoglobin: female <12 g/dL, male <13 g/dL

## DISCUSSION

This study examined associations between metabolic status and hemoglobin levels and presumptive TB risk among 58 Indonesian migrant workers in Johor Bahru, Malaysia. Using the expanded definition, 27.6% met the presumptive TB risk criteria. Compared with the no-risk group, participants with presumptive TB risk had significantly higher total cholesterol and fasting blood glucose levels, and total cholesterol ≥200 mg/dL was associated with an almost fourfold higher odds of meeting the presumptive TB criteria.

The prevalence of presumptive TB risk (27.6%) was substantially higher than the 9.0% found using the standard Ministry of Health Indonesia criteria (which requires cough ≥14 days or hemoptysis or cough with ≥2 systemic symptoms). This difference reflects the expanded definition's increased

sensitivity for detecting early or atypical TB presentations, which is particularly important in migrant populations where symptoms may be underreported or atypical.

This prevalence is consistent with systematic review findings by Chen et al. (2025), who reported TB prevalence among migrants of 214.52 per 100,000 population, with even higher rates among refugees and asylum seekers (439.25 per 100,000). The higher prevalence in migrant populations reflects their vulnerabilities including crowded living conditions (28.4% lived with >4 persons), occupational risks, and limited healthcare access (Mohd Putera et al., 2023; Rast et al., 2025). The most common symptom was cough (19.0%), followed by night sweats (13.8%). These findings align with classic TB presentation, where chronic respiratory symptoms predominate (Ministry of Health RI, 2023).

The most significant finding was the association between total cholesterol  $\geq 200$  mg/dL and presumptive TB risk (OR=3.67, 95% CI: 1.03-13.07,  $p=0.044$ ). Participants with presumptive TB risk also had significantly higher median cholesterol levels (207.5 vs 191.0 mg/dL,  $p=0.047$ ). This finding is biologically plausible and supported by recent literature. *Mycobacterium tuberculosis* is known to utilize host cholesterol for intracellular survival and replication within macrophages (Moopanar et al., 2023). The bacterium's cell wall is rich in mycolic acids and other lipids that contribute to virulence and immune evasion. Studies using UPLC-MS/MS have demonstrated that TB patients exhibit abnormal phospholipid, glyceride, and sphingolipid metabolism, with these abnormalities normalizing during successful treatment (Chen et al., 2021).

Furthermore, research by Brake et al. (2025) demonstrated that dyslipidemia in TB patients correlates with disease severity and inflammatory markers, and that atherogenic lipid profiles persist even after treatment completion. Kagemann et al. (2025) introduced the concept of metabolic scarring from TB infection, suggesting a bidirectional relationship between metabolic disorders and TB. Our findings support the hypothesis that dyslipidemia may both predispose individuals to TB and result from TB-related inflammation.

Our findings extend previous research on TB treatment outcomes by identifying metabolic risk factors at the pre-diagnosis stage. While Meiyanti et al. (2024) focused on factors influencing TB treatment success such as treatment duration and HIV status in West Nusa Tenggara, Indonesia, our study complements these findings by demonstrating that metabolic abnormalities (hypercholesterolemia and hyperglycemia) are already detectable in individuals with presumptive TB symptoms, long before treatment initiation. This suggests that metabolic screening could potentially identify high-risk individuals earlier, allowing for earlier intervention and closer monitoring during subsequent treatment.

Interestingly, our study found a stronger association with total cholesterol than with fasting blood glucose, despite extensive literature supporting diabetes as a TB risk factor. A Cochrane systematic review by Franco et al. (2024) reported that individuals with diabetes have 1.9 times higher risk for active TB, while Irawan et al. (2025) found that type 2 diabetes patients had 4.11 times greater risk for multidrug-resistant TB. The weaker association with glucose in our study

may be due to the relatively small sample size or the use of symptom-based rather than confirmatory TB diagnosis.

Although not reaching statistical significance in categorical analysis ( $p=0.247$ ), participants with presumptive TB risk had significantly higher median fasting blood glucose (104.0 vs 99.5 mg/dL,  $p=0.035$ ). This suggests a continuous relationship between glucose levels and TB symptoms, consistent with the established literature on diabetes-TB comorbidity. Mechanistically, hyperglycemia impairs host immune responses through multiple pathways: macrophage dysfunction, impaired cytokine production (reduced IFN- $\gamma$  and IL-12), increased T-cell apoptosis, impaired granuloma formation, and oxidative stress (Al-Bari et al., 2024). These mechanisms synergistically increase susceptibility to TB and worse clinical outcomes. The bidirectional relationship between diabetes and TB has important clinical implications. Boadu et al. (2024) emphasized the need for bidirectional screening, screening for TB in diabetic patients and screening for diabetes in TB patients particularly in high-risk populations like migrant workers.

This study found no significant association between hemoglobin levels and presumptive TB risk ( $p=0.710$ ). Only 12.5% of the TB risk group had low hemoglobin compared to 27.3% of the no-risk group. This contrasts with previous studies reporting high anemia prevalence in TB patients (Abaynew et al., 2023; Al-Bari, 2024). Several factors may explain this discrepancy. First, the presumptive TB cases in this study were identified based on symptoms rather than confirmed diagnosis, potentially representing earlier disease stages where anemia has not yet developed. Second, the nutritional status of this migrant worker population appeared relatively adequate (mean BMI 26.1 kg/m<sup>2</sup>). Third, none of the participants reported hemoptysis, which would directly cause blood loss anemia. Al-Bari et al. (2024) demonstrated that anemia in TB is associated with disease progression and occurs even before clinical symptoms appear, but this may require more advanced disease than captured by our symptom-based definition.

This occupational clustering is noteworthy, as teachers and education staff may have prolonged exposure to students in classroom settings, potentially facilitating TB transmission. Additionally, education sector workers in migrant contexts often share living arrangements and have close contact with children who may have undiagnosed TB. No significant differences were found for age, gender, education level, or length of employment, suggesting that metabolic parameters may be more important predictors of TB risk than demographic factors in this population.

The findings from this research reveal important directions for how tuberculosis programs can better serve migrant worker populations. A comprehensive approach to screening for migrant workers could meaningfully enhance early detection by incorporating metabolic assessments, with particular attention to lipid profiling as part of standard health screenings. Those individuals identified with hypercholesterolemia warrant more intensive symptom screening to capture potential TB cases earlier. Building on this foundation, providers working with migrant communities would benefit from

adopting a bidirectional screening strategy that addresses both tuberculosis and metabolic disorders simultaneously, recognizing that these health concerns frequently overlap within this vulnerable population (Boadu et al., 2024). This integrated approach reflects the interconnected nature of health challenges in migrant populations and allows for more efficient resource allocation.

Beyond screening practices, the research demonstrates that using an expanded symptom-based definition one that includes any respiratory symptom or two or more systemic symptoms successfully identifies more at-risk individuals compared to conventional diagnostic criteria. This broader approach proves particularly valuable in high-prevalence, hard-to-reach settings where traditional case-finding methods may fall short. Finally, implementing targeted health education initiatives for migrant workers that emphasize the critical relationship between metabolic health and susceptibility to infectious diseases can foster greater engagement in preventive health behaviors, ultimately strengthening both individual and community health resilience.

## **CONCLUSIONS AND RECOMMENDATIONS**

This study demonstrates that elevated total cholesterol is associated with increased presumptive TB risk among Indonesian migrant workers in Johor Bahru, Malaysia. Using an expanded definition ( $\geq 1$  respiratory symptom OR  $\geq 2$  systemic symptoms), 27.6% of participants met presumptive TB risk criteria. Participants with total cholesterol  $\geq 200$  mg/dL had 3.67 times higher risk of meeting presumptive TB criteria ( $p=0.044$ ). Hemoglobin levels showed no significant association. Provide some conclusions and the implementation of the Research results.

## **FURTHER STUDY**

This study has several limitations such as presumptive TB risk was defined using symptoms rather than confirmatory testing; no sputum microscopy, molecular testing, or chest X-ray was performed. Future research directions longitudinal studies with larger sample sizes, confirmatory TB diagnostics (GeneXpert, culture), comprehensive lipid profiling (HDL, LDL, triglycerides), and assessment of inflammatory markers would strengthen causal inference and provide deeper mechanistic insights into the metabolic-TB relationship in migrant populations. Integration of metabolic screening into TB case-finding protocols may enhance detection sensitivity. Migrant health screening programs might benefit from expanded protocols including lipid profiling alongside conventional TB symptom assessment. Health education initiatives should address the interconnections between metabolic health and infectious disease susceptibility, potentially motivating behavioral modifications and healthcare engagement.

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Hemoglobin and fasting glucose levels showed no significant association. Conclusion: Elevated total cholesterol is associated with heightened presumptive TB risk among Indonesian migrant workers. Metabolic screening, particularly lipid profiling, may enhance TB case detection in this vulnerable population.

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