Original article

Household contact as a key risk factor for latent tuberculosis infection among patients with diffuse large B-cell lymphoma

Piyapong Kanya[1], Worarat Imsanguan[2], Kittiya Maneechedtha[1] and Wirunrat Butkaew[3]

[1]Division of Hematology, Department of Internal Medicine; [2]Division of Pulmonary Diseases, Department of Internal Medicine; [3]Department of Pharmacy, Chiang Rai Prachanukroh Hospital

Abstract:

Introduction: *Patients with diffuse large B-cell lymphoma (DLBCL) have an increased risk of reactivating latent tuberculosis infection (LTBI) into active tuberculosis (TB) during chemotherapy or hematopoietic stem cell transplantation. However, extensive testing for LTBI among all patients is not practical, especially in regions with limited health resources.* ***Objective:*** *This study aimed to identify risk factors associated with an increased risk of LTBI among patients with newly diagnosed DLBCL and to determine the prevalence of LTBI in these patients.* ***Materials and Methods:*** *A retrospective cohort study of patients with newly diagnosed DLBCL was conducted at Chiang Rai Prachanukroh Hospital from September 2020 to June 2023. All patients were screened for LTBI using interferon-release assays (IGRAs), either the QuantiFERON-TB Gold In-Tube (QFT) or T-SPOT.TB (T-SPOT) tests, after DLBCL diagnosis and before the start of treatment. Data were collected from medical records. Generalized linear models were used to estimate the adjusted risk ratio (RR) and 95% confidence interval (CI) for LTBI risk factors.* ***Results:*** *A total of 127 patients with newly diagnosed DLBCL were enrolled, with a mean age of 59.17 years. Among them, 17 patients had IGRAs-proven LTBI, resulting in a prevalence of 13.39%. The results showed that household contact with TB significantly increased the risk of LTBI (adjusted RR: 3.24, 95%CI: 1.51-6.14).* ***Conclusion:*** *Patients with newly diagnosed DLBCL patients who had household contact with TB had a significantly higher risk of LTBI. These findings highlight the importance of targeted LTBI screening among patients with newly diagnosed DLBCL, particularly those with household contact with TB.*

Keywords : ● *Latent tuberculosis infection* ● *Diffuse large B-cell lymphoma* ● *Risk factor*

J Hematol Transfus Med. 2025;35:201-9.

Received 20 December 2024 Corrected 2 February 2025 Accepted 26 March 2025

Correspondence should be addressed to Piyapong Kanya, Division of Hematology, Department of Internal Medicine, Chiang Rai Prachanukroh Hospital

นิพนธ์ต้นฉบับ

ผู้สัมผัสวัณโรคร่วมบ้านเป็นปัจจัยเสี่ยงต่อการติดเชื้อวัณโรคระยะแฝงในผู้ป่วยมะเร็งต่อมน้ำเหลืองรายใหม่ชนิด diffuse large B-cell lymphoma

ปิยะพงษ์ กัญญา[1] วรรัตน์ อิ่มสงวน[2] กิตติยา มณีเชษฐา[1] และ วิรัญรัตน์ บุตรแก้ว[3]

[1]สาขาโลหิตวิทยา แผนกอายุรกรรม [2]สาขาโรคระบบการหายใจ แผนกอายุรกรรม [3]แผนกเภสัชกรรม โรงพยาบาลเชียงรายประชานุเคราะห์

บทคัดย่อ

บทนำ *ผู้ป่วยมะเร็งต่อมน้ำเหลืองชนิด diffuse large B-cell lymphoma (DLBCL) มีความเสี่ยงที่การติดเชื้อวัณโรคระยะแฝงกลายเป็นวัณโรค ระหว่างการรักษาด้วยยาเคมีบำบัดหรือปลูกถ่ายไขกระดูก* ***วัตถุประสงค์*** *หาปัจจัยที่สัมพันธ์กับการติดเชื้อวัณโรคระยะแฝงในผู้ป่วยมะเร็งต่อมน้ำเหลืองรายใหม่ชนิด DLBCL และความชุกของการติดเชื้อวัณโรคระยะแฝง* ***วัสดุและวิธีการ*** *ศึกษาย้อนหลัง ในโรงพยาบาลเชียงรายประชานุเคราะห์ ตั้งแต่เดือนกันยายน พ.ศ. 2563 ถึงเดือนมิถุนายน พ.ศ. 2566 ผู้ป่วยทุกรายได้รับการตรวจคัดกรองการติดเชื้อวัณโรคระยะแฝงด้วยวิธี interferon-release assays ก่อนเริ่มการรักษา วิเคราะห์ปัจจัยที่สัมพันธ์ต่อการติดเชื้อวัณโรคระยะแฝง โดย generalized linear models* ***ผลการศึกษา*** *ผู้ป่วยมะเร็งต่อมน้ำเหลืองรายใหม่ชนิด DLBCL จำนวน 127 ราย อายุเฉลี่ย 59.17 ปี ติดเชื้อวัณโรคระยะแฝง 17 ราย มีความชุกร้อยละ 13.39 โดยปัจจัยที่สัมพันธ์ต่อการติดเชื้อวัณโรคระยะแฝงอย่างมีนัยสำคัญทางสถิติคือผู้สัมผัสวัณโรคร่วมบ้าน โดยมีความเสี่ยงสัมพัทธ์เท่ากับ 3.24 และช่วงความเชื่อมั่นที่ร้อยละ 95 เท่ากับ 1.51 ถึง 6.14* ***สรุป*** *ผู้สัมผัสวัณโรคร่วมบ้าน เป็นปัจจัยที่สัมพันธ์ต่อการติดเชื้อวัณโรคระยะแฝงในผู้ป่วยมะเร็งต่อมน้ำเหลืองรายใหม่ชนิด DLBCL และควรตรวจคัดกรองการติดเชื้อวัณโรคระยะแฝงในผู้ป่วยที่มีความเสี่ยงดังกล่าว*

คำสำคัญ : ● *การติดเชื้อวัณโรคระยะแฝง* ● *ผู้ป่วยมะเร็งต่อมน้ำเหลืองชนิด diffuse large B cell lymphoma* ● *ปัจจัยเสี่ยง*

วารสารโลหิตวิทยาและเวชศาสตร์บริการโลหิต. 2568;35:201-9.

Introduction

Tuberculosis (TB) is a widespread communicable disease that remains a serious public health issue with high morbidity and mortality.[1] According to the World Health Organization (WHO), Thailand is a high-incidence country for TB with an estimated incidence rate of 157 per 100,000 population in 2023.[2-3] Chiang Rai is among the top ten provinces with a high incidence of TB, with a TB notification rate of 137 per 100,000 cases.[3-4] Latent tuberculosis infection (LTBI) is defined as a state of persistent *Mycobacterium tuberculosis (M. tuberculosis)*-specific T cell responses without clinical evidence of TB.[5] Approximately one-third of the global population is infected with *M. tuberculosis*, and most infected individuals exhibit no signs or symptoms of TB.[6-7] The incidence of LTBI in Thailand and Chiang Rai Province is unknown but is presumed to be relatively high, particularly among high-risk populations such as healthcare workers and prisoners.[8-9] Although individuals with LTBI do not transmit the disease, 5% to 10% may develop active TB during their lifetime.[10-11] The risk of TB reactivation is increased among patients with lymphoma due to malnutrition and diminished immune functioning, both as a direct consequence of the disease and as a result of chemotherapy.[12-13] Patients with lymphoma have a significantly higher risk of developing TB, with an estimated relative risk of 2 to 40 times that of the general population.[14-15] The WHO has published guidelines for the programmatic management of LTBI,[16] which provide a comprehensive approach to LTBI screening using either the tuberculin skin test (TST) or interferon-gamma release assays (IGRAs), treatment, and management. These guidelines prioritize screening among individuals at the highest risk of developing active TB, including people living with human immunodeficiency virus (HIV), infants and children under five years of age with household exposure to pulmonary TB, and other at-risk HIV-negative populations such as patients initiating anti-tumor necrosis factor (TNF) therapy, patients undergoing dialysis, individuals preparing for organ or hematopoietic stem cell transplantation and patients with silicosis.[17-20]

The Thai Lymphoma Study Group (TLSG) reported that diffuse large B-cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma (NHL), accounting for 58.1% of cases.[21] Patients with DLBCL have an increased risk of TB due to immune deficiencies that impaired the body's ability to fight TB and the potential reactivation of LTBI during chemotherapy or hematologic stem cell transplantation.[22-23] Currently, no studies or official recommendations exist for LTBI screening among patients with DLBCL. However, extensive LTBI testing for all patients is not practical, especially in regions with limited healthcare resources. This study aimed to identify factors associated with LTBI in patients with newly diagnosed DLBCL to facilitate effective screening and determine the prevalence of LTBI among these patients.

Materials and methods

Study design

A retrospective cohort study of newly diagnosed DLBCL patients was conducted at Chiang Rai Prachanukroh Hospital from September 2020 to June 2023. Data were collected from medical records and obtained from the Chiang Rai Prachanukroh Hospital databases. The study protocol was approved by the Ethics Committee of Chiang Rai Prachanukroh Hospital (EC CRH 075/66 In) and was carried out in accordance with the Declaration of Helsinki.

Participants

This study included patients aged 18 years or older who had been newly diagnosed with DLBCL according to the WHO 2016 classification of lymphoid neoplasms criteria.[24] All patients were screened for LTBI using IGRAs after DLBCL diagnosis and before the start of treatment, specifically with the QuantiFERON-TB Gold In-Tube (QFT) or T-SPOT.TB (T-SPOT) tests. Screening for LTBI in adults using IGRAs has shown moderate sensitivity (81-90%) and high specificity (95-99%).[25]

Patients with prior TB infection were excluded from the study. DLBCL patients with a positive QFT or T-SPOT test result were classified as having LTBI, while those with negative results were classified as not having LTBI. A household contact with TB was defined as a person who shared the same enclosed living space with a patient with pulmonary TB for one or more nights or for frequent or extended daytime periods during the three months before the start of current treatment.[26] The risk ratio of IGRA-proven LTBI in DLBCL is unknown. However, solid cancers and hematologic malignancies are known to increase the risk of LTBI by approximately 1-2 times.[27-29] Based on this data, we used a risk ratio of 2 for IGRA-proven LTBI in DLBCL. Sample size calculation was performed using a Cox proportional hazards model with a significance level (α) of 0.05, a power of 85%, and a sample loss rate of 20%, resulting in a required sample size of at least 94 patients.

Objective

The primary objective was to identify risk factors associated with an increased risk of LTBI among patients with newly diagnosed DLBCL. The secondary objective was to determine the prevalence of LTBI in these patients.

Statistical analysis

Statistical analysis was performed using a STATA, Version 14. Descriptive statistics were used to present the data, including numbers and percentages for categorical variables. The mean and standard deviation (SD) were used for normally distributed continuous variables, while the median and interquartile range (IQR) were used for non-normally distributed continuous variables. Categorical variables were compared using the exact probability test as appropriate. The t-test was used for comparison of normally distributed data, and the Wilcoxon rank-sum (Mann-Whitney) test was used for non-normally distributed data. Univariate analysis and generalized linear models were used to estimate the crude relative risk (RR) and adjusted RR, respectively, along with the 95% confidence interval (CI) for the risk factors of LTBI among patients with newly diagnosed DLBCL. All variables with statistical significance from the univariate analysis were selected for multivariate analysis. A *p-value* of 0.05 was considered statistically significant.

Results

The study included 127 patients with newly diagnosed DLBCL with a mean age of 59.17 years, between September 2020 and June 2023. The majority of cases comprised patients with DLBCL, not otherwise specified (NOS), accounting for 81 of 127 patients (63.78%). All patients with newly diagnosed DLBCL were screened for LTBI using IGRAs with either the QFT or T-SPOT tests. Data collection was comprehensive, without any missing data. Among them, 17 patients had IGRAs-proven LTBI, resulting in a prevalence of 13.39%. The prevalence of LTBI was significantly higher among males than females [13 (76.47%) vs. 54 (49.09%), *p-value* = 0.040], among those with household contact with TB [5 (29.41%) vs. 1 (0.91%), *p-value* < 0.001], and those with absence of a Bacillus Calmette-Guérin (BCG) scar [5 (29.41%) vs. 6 (5.45%), *p-value* = 0.007]. Table 1 summarizes the clinical characteristics of DLBCL patients with and without LTBI. No differences were observed between the groups regarding their baseline clinical characteristics, comorbidities (including diabetes, HIV and chronic kidney disease), and laboratory results.

Risk factors for LTBI among patients with DLBCL are shown in Table 2. Univariate analysis indicated that the risk factors associated with LTBI in DLBCL patients included male gender (crude RR: 2.91, 95%CI: 1.00-8.44), household contact with TB (crude RR: 8.40, 95%CI: 4.41-16.02) and absence of a BCG scar (crude RR: 4.40, 95%CI: 1.90-10.18). However, multivariate regression analysis of male, household contact with TB and absence of a BCG scar showed that the only risk factor associated with significantly increased risk of LTBI was household contact with TB (adjusted RR: 3.24, 95%CI: 1.51-6.14).

Table 1 Clinical characteristics of diffuse large B-cell lymphoma patients with latent tuberculosis infection (LTBI).

Factors	Total patients with DLBCL 127 (100%)	Patients with DLBCL and LTBI 17 (13.39%)	Patients with DLBCL without LTBI 110 (86.61%)	*p*-value
Age (years) mean (±SD)	59.17 (±14.10)	56.29 (±12.04)	59.61 (±14.39)	0.369
Male	67 (52.76)	13 (76.47)	54 (49.09)	0.040
B symptoms	98 (77.17)	12 (70.59)	86 (78.18)	0.537
Household contact with tuberculosis	6 (4.72)	5 (29.41)	1 (0.91)	< 0.001
Absence of a BCG scar	11 (8.66)	5 (29.41)	6 (5.45)	0.007
ECOG performance status				
- 0-1 score	63 (49.61)	11 (64.71)	52 (47.27)	0.141
- 2-4 score	64 (50.39)	6 (35.29)	58 (52.73)	0.203
Bulky disease or lesion ≥ 7.5 cm	21 (16.54)	3 (17.65)	18 (16.36)	1.000
Ann Arbor stage				
- I-II	52 (40.94)	8 (47.06)	44 (40)	0.384
- III-IV	75 (59.06)	9 (52.94)	66 (60)	0.605
DLBCL subtype				
- Activated B-cell	37 (29.13)	5 (29.41)	32 (29.09)	1.000
- Germinal center B-cell	9 (7.09)	2 (11.76)	7 (6.36)	0.345
- Not otherwise specified	81 (63.78)	10 (58.82)	71 (64.55)	0.787
International Prognostic Index				
- Low (0-1 score)	43 (33.86)	8 (47.06)	35 (31.82)	0.272
- Low intermediate (2 score)	18 (14.17)	4 (23.53)	14 (12.73)	0.262
- High intermediate (3 score)	39 (30.71)	2 (11.76)	37 (33.64)	0.091
- High (4-5 score)	27 (21.26)	3 (17.65)	24 (21.82)	1.000
Comorbidity				
- Diabetes mellitus	11 (8.66)	2 (11.76)	9 (8.18)	0.642
- HIV infection	5 (3.94)	1 (5.88)	4 (3.64)	0.519
- Chronic kidney disease	34 (26.77)	4 (23.53)	30 (27.27)	1.000
Elevated serum lactate dehydrogenase	78 (61.42)	9 (52.94)	69 (62.73)	0.438
Hemoglobin (g/dl) mean (±SD)	10.79 (±2.24)	11.68 (±2.38)	10.65 (±2.19)	0.080
White blood cell ($x10^9$/L) median (IQR)	8.30 (6.10-11.21)	9 (6.70-9.90)	8.25 (5.90-11.21)	0.407
Neutrophil (%) median (IQR.)	68 (60-80.50)	63 (56.70-79.80)	68 (61.20-80.50)	0.486
Lymphocyte (%) median (IQR.)	20 (9.20-27)	21 (9.90-28.50)	19.85 (9.20-26.10)	0.846
Platelet ($x10^9$/L) median (IQR.)	311 (237-386)	291 (241-395)	314 (237-385)	0.876

BCG, Bacillus Calmette-Guérin; ECOG, Eastern Cooperative Oncology Group; DLBCL, diffuse large B-cell lymphoma; International Prognostic Index score including age more than 60 years, performance status assessment using ECOG Score 2-4, Ann Arbor stage III-IV, extranodal involvement more than 1 site and serum lactate dehydrogenase more than upper normal limit; HIV, Human immunodeficiency virus; SD, standard deviation; IQR, interquartile range.

Table 2 Risk factors for latent tuberculosis infection (LTBI) among patients with diffuse large B-cell lymphoma

	Univariate		Multivariate	
	Crude RR	**95%CI**	**Adjusted RR**	**95%CI**
Age				
< 40 years (reference)	1	-		
40-60 years	0.86	0.22-3.33		
> 60 years	0.86	0.22-3.33		
Male	2.91	1.00-8.44	1.27	-0.47-2.17
B symptoms	0.71	0.27-1.85		
Household contact with tuberculosis	8.40	4.41-16.02	3.24	1.51-6.14
Absence of a BCG scar	4.40	1.90-10.18	2.73	0.58-3.52
ECOG performance status 2-4 score	0.54	0.21-1.36		
Bulky disease or lesion ≥ 7.5 cm	1.08	0.34-3.44		
Ann Arbor stage I-II	1.28	0.53-3.10		
DLBCL subtype				
Activated B-cell	1.23	0.50-3.02		
Germinal center B-cell	1.23	0.50-3.02		
Not otherwise specified (reference)	1	-		
International Prognostic Index 0-2 score	2.60	0.97-6.94		
Comorbidity				
Diabetes mellitus	1.41	0.37-5.37		
HIV	1.52	0.25-9.33		
Chronic kidney disease	0.84	0.29-2.40		

RR, relative risk; CI, confidence interval; BCG, Bacillus Calmette-Guérin; ECOG, Eastern Cooperative Oncology Group; DLBCL, diffuse large B-cell lymphoma; LTBI, latent tuberculosis infection; International Prognostic Index score including age more than 60 years, performance status assessment using ECOG Score 2-4, Ann Arbor stage III-IV, extranodal involvement more than 1 site and serum lactate dehydrogenase more than upper normal limit; HIV, Human immunodeficiency virus.

Discussion

This study highlights the significant association between household contact with TB and the risk of LTBI among patients with newly diagnosed DLBCL. Implementing targeted LTBI screening and preventive measures in this high-risk population is crucial for reducing TB morbidity and improving patient outcomes. The strengths of this study include its focus on patients with DLBCL, which is the most common hematologic malignancy and the most frequent subtype of NHL. However, the study has limitations, including the absence of data collection on some potential risk factors for LTBI, such as smoking status, occupational or workplace exposures, and history of BCG vaccination.

There are two diagnostic tests for LTBI: the TST and the two techniques of IGRAs, which measure in vitro the release of interferon-gamma (IFN-γ) produced by T-lymphocytes against the stimulation of highly specific antigens of *M. tuberculosis*: QFT and T-SPOT. For T-SPOT, the process is more protracted because prior separation of the lymphocyte is required, whereas for QFT, only a simple ESISA is needed.[30-31] Currently, no gold standard test exists for diagnosing LTBI, and it is estimated that approximately 20% to 30% of the world's population is infected with *M. tuberculosis*.[32-33] The two main tests used for LTBI screening are the IGRAs and the TST. Both tests have their strengths and limitations, and their accuracy can vary based on factors such as

the patient's immune status and the prevalence of TB in the population.[34] In this study, only 13.39% of DLBCL patient exhibited IGRAs-proven LTBI. Several reasons may explain the low detection rate of LTBI using IGRA among DLBCL patients. Active lymphoma can lead to low immune responses, a reduced number of lymphocytes, and the need for chemotherapy. In particular, corticosteroid use can suppress the immune system, leading to false-negative results.[35] However, the use of IGRA for screening LTBI in DLBCL patients proved effective in identifying those at risk. This supports the recommendation of IGRAs or TST as a reliable method for LTBI screening in high-risk populations, as endorsed by the WHO.[16]

In our study, household contact with TB was found to be a significant risk factor for LTBI among patients with DLBCL, with a three-fold higher risk compared to the general population. This suggests that close contact with patients with TB is a critical route of transmission, particularly for immunocompromised individuals such as those with DLBCL. Household contact with TB increases the risk of LTBI due to prolonged exposure to infectious agents, as the bacteria are inhaled through aerosols, especially in enclosed spaces.[36-37] This data is consistent with previous studies that identified household contacts with TB patients as a high-risk group for LTBI. Research has shown that prolonged exposure to TB patients increases the risk of LTBI, with additional factors such as exposure to an index case with a high bacterial load (e.g., cavitation on chest radiograph or a high sputum smear grade), sharing a bedroom and frequent interactions with TB patients contributing to the risk.[38-39] Additionally, this is particularly relevant for DLBCL patients, who are already immunocompromised and more susceptible to infections.[29,40] The univariate analysis identified male sex as a risk factor for LTBI, although this association did not persist in the adjusted analysis. However, some studies report that males are more likely to develop LTBI than females.[41-42] The higher risk is attributed to the fact that men often engage in outdoor activities that carry a higher risk.[43-44] While the absence of a BCG scar was identified as a risk factor in the univariate analysis, it did not remain significant in the adjusted analysis. Several studies have found that BCG vaccination is associated with a lower risk of LTBI,[45-47] and the absence of a BCG scar has been linked to an increased occurrence of LTBI.[48] The BCG vaccine may decrease the risk of LTBI primarily because it provides early protection against *M. tuberculosis*.[49] However, most studies report that the protective effect of BCG vaccination lasts for only 10 to 15 years.[50-51]

Prevention of active TB disease by screening and treating LTBI is a critical component of the WHO End TB Strategy.[52] These findings highlight the importance of targeted LTBI screening among patients with newly diagnosed DLBCL, particularly those with household contact with TB. Further research is needed to refine screening recommendations for this high-risk group.

Conclusion

Newly diagnosed DLBCL patients with household contact with TB had a significant association with LTBI. These findings highlight the importance of targeted LTBI screening in newly diagnosed DLBCL patients, particularly those with household contact with TB.

Acknowledgement

The authors would like to thank the Department of Medicine and Department of Human Resources of Chiang Rai Prachanukroh Hospital, Thailand for the data contribution.

Competing interests: This study has no competing interests

Funding: This study has been fully supported by Chiang Rai Prachanukroh Hospital, Thailand

Reference

1. Reid MJA, Arinaminpathy N, Bloom A, Bloom BR, Boehme C, Chaisson R, et al. Building a tuberculosis-free world: The Lancet Commission on tuberculosis. Lancet. 2019;393:1331-84.
2. Global tuberculosis report 2024. Geneva: World Health Organization; 2024.
3. Division of Tuberculosis. National Tuberculosis Control Programme Guideline, Thailand 2021. Bangkok: Division of Tuberculosis; 2021.
4. Report on the situation of tuberculosis. Chiang Rai Provincial Public Health. 2024
5. Mack U, Migliori GB, Sester M, Rieder HL, Ehlers S, Goletti D, et al. LTBI: latent tuberculosis infection or lasting immune responses to M. tuberculosis? A TBNET consensus statement. Eur Respir J. 2009;33:956-73.
6. Dye C, Scheele S, Dolin P, Pathania V, Raviglione MC. Consensus statement. Global burden of tuberculosis: estimated incidence, prevalence, and mortality by country. WHO Global Surveillance and Monitoring Project. JAMA. 1999;282:677-86.
7. Global Tuberculosis Report. Geneva, Switzerland: World Health Organization; 2015.
8. Gatechompol S, Harnpariphan W, Supanan R, Suwanpimolkul G, Sophonphan J, Ubolyam S, et al. Prevalence of latent tuberculosis infection and feasibility of TB preventive therapy among Thai prisoners: a cross-sectional study. BMC Public Health. 2021;21:1206.
9. Nonghanphithak D, Reechaipichitkul W, Chaiyasung T, Faksri K. Risk factors for latent tuberculosis infection among health-care workers in Northeastern Thailand. Southeast Asian J Trop Med Public Health. 2016;47:1198-208.
10. Global Tuberculosis Report. Geneva, Switzerland: World Health Organization; 2023.
11. Comstock GW, Livesay VT, Woolpert SF. The prognosis of a positive tuberculin reaction in childhood and adolescence. Am J Epidemiol. 1974;99:131-8.
12. Bourke CD, Berkley JA, Prendergast AJ. Immune Dysfunction as a Cause and Consequence of Malnutrition. Trends Immunol. 2016;37:386-98.
13. Dobler CC, Cheung K, Nguyen J, Martin A. Risk of tuberculosis in patients with solid cancers and haematological malignancies: a systematic review and meta-analysis. Eur Respir J. 2017;50:1700157.
14. Anibarro L, Pena A. Tuberculosis in patients with haematological malignancies. Mediterr J Hematol Infect Dis. 2014;6:e2014026.
15. Ganzel C, Silverman B, Chemtob D, Ben Shoham A, Wiener-Well Y. The risk of tuberculosis in cancer patients is greatest in lymphoma and myelodysplastic syndrome/myeloproliferative neoplasm: a large population-based cohort study. Leuk Lymphoma. 2019;60:720-5.
16. Latent tuberculosis infection: updated and consolidated guidelines for programmatic management. Geneva, Switzerland: World Health Organization; 2018.
17. Guidelines on the management of latent tuberculosis infection. Geneva, Switzerland: World Health Organization; Guidelines update date: 2020.
18. Lee SK, Kim SY, Kim EY, Jung JY, Park MS, Kim YS, et al. Mycobacterial infections in patients treated with tumor necrosis factor antagonists in South Korea. Lung. 2013;191:565-71.
19. Recommendations for investigating contacts of persons with infectious tuberculosis in low- and middle-income countries. Geneva, Switzerland: World Health Organization. 2012.
20. Guidelines for intensified tuberculosis case-finding and isoniazid preventive therapy for people living with HIV in resource-constrained settings. Geneva, Switzerland: World Health Organization. 2011.
21. Intragumtornchai T, Bunworasate U, Wudhikarn K, Lekhakula A, Julamanee J, Chansung K, et al. Non-Hodgkin lymphoma in South East Asia: An analysis of the histopathology, clinical features, and survival from Thailand. Hematol Oncol. 2018;36:28-36.
22. Cheon J, Kim C, Park EJ, Ock M, Lee H, Ahn JJ, et al. Active tuberculosis risk associated with malignancies: an 18-year retrospective cohort study in Korea. J Thorac Dis. 2020;12:4950-9.
23. Chen CY, Sheng WH, Cheng A, Tsay W, Huang SY, Tang JL, et al. Clinical characteristics and outcomes of Mycobacterium tuberculosis disease in adult patients with hematological malignancies. BMC Infect Dis. 2011;11:324.
24. Swerdlow SH, Campo E, Pileri SA, Harris NL, Stein H, Siebert R, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood. 2016;127:2375-90.
25. Jonas DE, Riley SR, Lee LC, Coffey CP, Wang SH, Asher GN, et al. Screening for Latent Tuberculosis Infection in Adults: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA. 2023;329:1495-509.
26. Getahun H, Matteelli A, Abubakar I, Aziz MA, Baddeley A, Barreira D, et al. Management of latent Mycobacterium tuberculosis infection: WHO guidelines for low tuberculosis burden countries. Eur Respir J. 2015;46:1563-76.
27. Mortezazadeh M, Karimi M, Esfandbod M, Mofidi A, Hemmati N, Kashani M, et al. Investigation of the prevalence of latent tuberculosis in cancer patients compared to non-cancer patients: a case-control study. Oncol Rev. 2024;18:1445678.
28. Bourlon C, Camacho-Hernández R, Fierro-Angulo OM, Acosta-Medina AA, Bourlon MT, Niembro-Ortega MD, et al. Latent Tuberculosis in Hematopoietic Stem Cell Transplantation: Diagnostic and Therapeutic Strategies to Prevent Disease Activation in an Endemic Population. Biol Blood Marrow Transplant. 2020;26:1350-4.
29. Osorio-López EA, Vilar-Compte D, García-Tirado J, Martin-Onraet A. Prevalence of latent tuberculosis in patients with hematological neoplasms in a cancer referral hospital in Mexico City. BMC Infect Dis. 2021;21:510.
30. Pai M, Denkinger CM, Kik SV, Rangaka MX, Zwerling A, Oxlade O, et al. Gamma interferon release assays for detection of Mycobacterium tuberculosis infection. Clin Microbiol Rev. 2014;27:3-20.

31. *Pai M, Riley LW, Colford JM Jr. Interferon-gamma assays in the immunodiagnosis of tuberculosis: a systematic review. Lancet Infect Dis. 2004;4:761-6.*
32. *Houben RM, Dodd PJ. The Global Burden of Latent Tuberculosis Infection: A Re-estimation Using Mathematical Modelling. PLoS Med. 2016;13:e1002152.*
33. *Cheng MP, Abou Chakra CN, Yansouni CP, Cnossen S, Shrier I, Menzies D, et al. Risk of Active Tuberculosis in Patients with Cancer: A Systematic Review and Meta-Analysis. Clin Infect Dis. 2017;64:635-44.*
34. *Auguste P, Tsertsvadze A, Pink J, Court R, McCarthy N, Sutcliffe P, et al. Comparing interferon-gamma release assays with tuberculin skin test for identifying latent tuberculosis infection that progresses to active tuberculosis: systematic review and meta-analysis. BMC Infect Dis. 2017;17:200.*
35. *González-Moreno J, García-Gasalla M, Losada-López I, Cifuentes Luna C, Mir Viladrich I, Fernández-Baca V, et al. IGRA testing in patients with immune-mediated inflammatory diseases: which factors influence the results? Rheumatol Int. 2018;38:267-73.*
36. *Rao M, Ippolito G, Mfinanga S, Ntoumi F, Yeboah-Manu D, Vilaplana C, et al. Latent TB Infection (LTBI) - Mycobacterium tuberculosis pathogenesis and the dynamics of the granuloma battleground. Int J Infect Dis. 2019;80S:S58-S61.*
37. *Karbito K, Susanto H, Adi MS, Sulistiyani S, Handayani OWK, Sofro MAU. Latent tuberculosis infection in family members in household contact with active tuberculosis patients in Semarang City, Central Java, Indonesia. J Public Health Afr. 2022;13:2157.*
38. *Faiz JF, Hadi EN. Risk Factors for Latent Tuberculosis Infection (LTBI) Among Household contacts with TB Patients: A Systematic Review. JIKM [Internet]. 2024;15:288-302.*
39. *Tornee S, Kaewkungwal J, Fungladda W, Silachamroon U, Akarasewi P, Sunakorn P. Risk factors for tuberculosis infection among household contacts in Bangkok, Thailand. Southeast Asian J Trop Med Public Health. 2004;35:375-83.*
40. *Lee SJ, Lee SH, Kim YE, Cho YJ, Jeong YY, Kim HC, et al. Risk factors for latent tuberculosis infection in close contacts of active tuberculosis patients in South Korea: a prospective cohort study. BMC Infect Dis. 2014;14:566.*
41. *Sayuti NASA, Ibrahim FW, Jufri NF, Masre SF, Abdullah AHA, Raub SHA, et al. Retrospective data analysis on the prevalence and demographic risk factors for latent tuberculosis infection (LTBI) cases from a private laboratory in Malaysia. Trop Biomed. 2024;41:257-63.*
42. *Nababan B, Triasih R, Chan G, Dwihardiani B, Hidayat A, Dewi SC, et al. The Yield of Active Tuberculosis Disease and Latent Tuberculosis Infection in Tuberculosis Household Contacts Investigated Using Chest X-ray in Yogyakarta Province, Indonesia. Trop Med Infect Dis. 2024;9:34.*
43. *Djibougou DA, Mensah GI, Sagna T, Sawadogo LT, Ouedraogo AK, Kabore A, et al. Magnitude and associated factors of latent tuberculosis infection due to Mycobacterium tuberculosis complex among high-risk groups in urban Bobo-Dioulasso, Burkina Faso. IJID Reg. 2022;4:1-9.*
44. *Ncayiyana JR, Bassett J, West N, Westreich D, Musenge E, Emch M, et al. Prevalence of latent tuberculosis infection and predictive factors in an urban informal settlement in Johannesburg, South Africa: a cross-sectional study. BMC Infect Dis. 2016;16:661.*
45. *Katelaris AL, Jackson C, Southern J, Gupta RK, Drobniewski F, Lalvani A, et al. Effectiveness of BCG Vaccination Against Mycobacterium tuberculosis Infection in Adults: A Cross-sectional Analysis of a UK-Based Cohort. J Infect Dis. 2020;221:146-55.*
46. *Wang PH, Lin SY, Liou HH, Chen CC, Shu CC, Lee CY, et al. Protective Effect of BCG and Neutrophil-to-Lymphocyte Ratio on Latent Tuberculosis in End Stage Renal Disease. Infect Dis Ther. 2023;12:1907-20.*
47. *Huang W, Fang Z, Luo S, Lin S, Xu L, Yan B, et al. The effect of BCG vaccination and risk factors for latent tuberculosis infection among college freshmen in China. International Journal of Infectious Diseases : IJID : Official Publication of the International Society for Infectious Diseases. 2022;122:321-26*
48. *Chanpho P, Chaiear N, Kamsa-Ard S. Factors Associated with Latent Tuberculosis Infection among the Hospital Employees in a Tertiary Hospital of Northeastern Thailand. Int J Environ Res Public Health. 2020;17:6876.*
49. *Dockrell HM, Smith SG. What Have We Learnt about BCG Vaccination in the Last 20 Years? Front Immunol. 2017;8:1134.*
50. *Andersen P, Doherty TM. The success and failure of BCG - implications for a novel tuberculosis vaccine. Nat Rev Microbiol. 2005;3:656-62.*
51. *Abubakar I, Pimpin L, Ariti C, Beynon R, Mangtani P, Sterne JA, et al. Systematic review and meta-analysis of the current evidence on the duration of protection by bacillus Calmette-Guérin vaccination against tuberculosis. Health Technol Assess. 2013;17:1-372, v-vi.*
52. *Implementing the end TB strategy: the essentials, 2022 update. Geneva: World Health Organization; 2022.*