Article published online: 2024-04-26

Original Article

Active Tuberculosis Risk Associated with Malignancies: A 4-Year Retrospective Study in a Tertiary Care Hospital

Priyamvada Roy[1] Kiran Bala[1] Jaya Biswas[1] Javed Ahmed[1] Raunak Bir[1] Vishwanath Yadav[1] Ashit Xess[1] Sanjana Kumari[1] Prabhat Singh Malik[2] S. V. S. Deo[3] Atul Batra[2] Atul Sharma[2] Urvashi B. Singh[1]

[1] Department of Microbiology, All India Institute of Medical Sciences, New Delhi, India
[2] Department of Medical Oncology, All India Institute of Medical Sciences, New Delhi, India
[3] Department of Surgical Oncology, All India Institute of Medical Sciences, New Delhi, India

Address for correspondence Urvashi B. Singh, MBBS, MD, Department of Microbiology, All India Institute of Medical Sciences, New Delhi 110029, India (e-mail: drurvashi@gmail.com).

South Asian J Cancer

Abstract

Priyamvada Roy

Background Tuberculosis (TB) remains an important public health problem worldwide. Risk of acquiring TB in patients diagnosed with cancers remains high and can result due to reactivation or reinfection. We share the experience in a large tertiary care hospital.

Materials and Methods Clinical samples from presumptive TB patients while on cancer therapy were tested by smear Ziehl–Neelsen (ZN) staining, GeneXpert MTB/RIF (Gx), TB polymerase chain reaction (PCR), and liquid culture (MGIT 960) from January 1, 2019, to December 31, 2022.

Statistical Analysis Stata 14.0 software was used for statistical analysis. The *p*-value calculation was done by Pearson's chi-square test.

Results Of 906 patients investigated, 42 (4.64%) tested positive for TB. Seven (1.37%) tested positive by ZN staining, 10 patients (6%) had culture positive by MGIT, 20 (10.53%) and 5 (13.51%) samples were positive by Gx and PCR, respectively. Maximum number of TB-positive patients were found to be suffering from carcinoma lung (28%) followed by leukemia (25%), gastrointestinal cancer (13%), and genitourinary cancer (13%), respectively. Seven of the 42 patients succumbed to the disease; the cases belonged to Hodgkin's lymphoma (75% mortality), leukemia (30% mortality), and genitourinary cancer (20% mortality).

Conclusion The incidence of active TB is high in cancer patients, especially lung cancer, leukemia, gastrointestinal, and genitourinary cancers. Mortality was high in Hodgkin's lymphoma patients who developed TB. Screening for TB at the time of diagnosis of a high TB risk cancer would help initiate early treatment. We recommend targeted screening for TB in patients with these high-risk cancers, at the time of diagnosis and periodically through cancer treatment.

Keywords
- GeneXpert
- lung cancer
- MGIT 960
- TB PCR
- Ziehl–Neelsen stain

DOI https://doi.org/10.1055/s-0044-1786363 ISSN 2278-330X

How to cite this article: Roy P, Bala K, Biswas J, et al. Active Tuberculosis Risk Associated with Malignancies: A 4-Year Retrospective Study in a Tertiary Care Hospital. South Asian J Cancer 2024;00(00):00–00.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

Introduction

Tuberculosis (TB) remains an important public health problem worldwide.[1] Latent TB infection (LTBI) defines the condition wherein an individual is infected with *Mycobacterium tuberculosis* (MTB) but not presently manifesting active disease.[1,2] For a person with documented LTBI, the projected lifetime risk of developing active TB is 10%, although preventive treatment can prevent this risk and confer a projected protective effect of 60 to 90%.[1,3,4] To decrease both the incidence of active TB and the associated screening costs, LTBI screening is applied selectively to those with high risk of developing active TB.[1] However, target populations for screening vary among countries and guidelines.[1,2,5–8]

Patients with malignancy may exhibit deficits in cell-mediated immunity as either a direct effect or an indirect effect related to chemotherapy.[1,9,10] Healthy individuals can harbor LTBIs for their entire lives, but in around 5 to 15% of infected individuals, TB disease can be reactivated.[11,12] Immunocompromised people are at increased risk of reactivation of LTBIs, which include patients with hematological malignancies and patients undergoing immunosuppressant cancer therapies such as chemotherapy.[13]

Accordingly, many patients with LTBI and cancer develop active TB.[1,14,15] However, the 2018 World Health Organization (WHO) guidelines do not recommend LTBI screening for patients with cancer.[16] Nonetheless, the WHO guidelines also highlight the importance of further research on the benefits and harms of LTBI screening in this patient population.[1,17]

Accurately calculating the magnitude of active TB risk faced by patients with various malignancies remains challenging.[1] A recent meta-analysis by Cheon et al reported an increased risk of TB development in patients with solid cancers, particularly hematologic, head and neck, and lung cancers.[1] Consequently, those patients faced a greater risk of developing active TB and would benefit from LTBI screening and treatment.[1,18] Dobler et al further performed a meta-analysis estimating the incidence of TB relative to a reference group after adjusting for age, and found that the incidence rate ratio of TB associated with cancer was 2.61; those authors concluded that LTBI screening in patients with cancer may be needless except for patients with hematologic malignancies and children with cancer.[1,13] Nair et al, Nanthanangkul et al, and Shu et al have also reported high prevalence of TB among cancer patients.[19–21] ►Table 1 lists the different studies on prevalence of TB in cancer patients.

The precision and dependability of TB diagnoses are often doubtful, as many clinical diagnoses of TB are not confirmed using microbiological evidence such as cultures or molecular methods including polymerase chain reaction (PCR).[1] Given the lack of studies exploring associations of active TB with several types of malignancies in a single population, as well as the contradictory results of previous studies, further research is needed to better define high-risk patients with malignancies.[1] In this study, we aimed to find out if there is risk of active TB in patients with malignancy.

Materials and Methods

Objective of the Study

The objective of the study was to evaluate the risk of active TB in patients with various cancers in a 2,478 bedded tertiary care hospital. The study was approved by the institutional ethical committee.

Inclusion Criteria

Inclusion criteria are cancer patients suspected to be suffering from TB.

Exclusion Criteria

There are no exclusion criteria.

Methods

Samples received from cancer patients during the period January 1, 2019, to December 31, 2022, on suspicion of presumptive TB for Ziehl–Neelsen (ZN) staining, GeneXpert MTB/RIF (Gx), TB PCR, and MGIT 960 were considered in the present study. Samples were processed by the n-acetyl L-cysteine (NALC)-sodium hydroxide (NaOH) method, that is, treatment of clinical samples with NALC, 4% NaOH, and sodium citrate for 15 minutes followed by neutralization

Table 1 Studies on prevalence of TB among cancer patients

S. no.	Article	Year	Author	Prevalence of TB among cancer patients (%)
1	Impact of active tuberculosis on treatment decisions in cancer	2021	Nair et al	0.17
2	Active tuberculosis risk associated with malignancies: an 18-year retrospective cohort study in Korea	2020	Cheon et al	0.535
3	Incidence of and risk factors for tuberculosis among cancer patients in endemic area: a regional cohort study	2020	Nanthanangkul et al	0.42186
4	The burdens of tuberculosis on patients with malignancy: incidence, mortality and relapse	2019	Shu et al	1.8
5	Risk of tuberculosis in patients with solid cancers and haematological malignancies: a systematic review and meta-analysis	2017	Dobler et al	0.0261

Abbreviation: TB, tuberculosis.

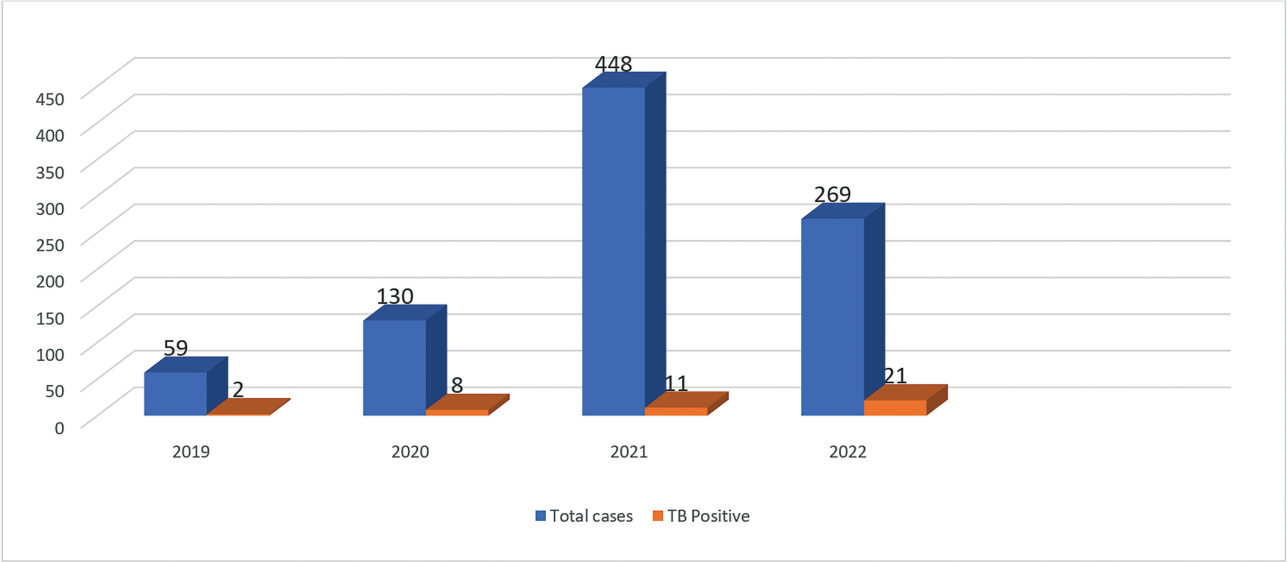

Fig. 1 Yearwise distribution of total number of cases and tuberculosis (TB)-positive cases.

with phosphate-buffered saline and centrifugation at 3,000 rpm for 30 minutes. The samples were subjected to four tests—microscopy (ZN staining), GeneXpert MTB/RIF (Gx), TB PCR, and liquid culture (MGIT 960).[22]

Decontaminated samples were stained by ZN technique. Reporting was done as per the National Tuberculosis Elimination Program guidelines.[23]

After processing the sample, concentrated sediment was inoculated into MGIT 960 medium and incubated at 37°C. It is a liquid medium for mycobacterial culture. A fluorescent compound is embedded in silicone on the bottom of each of the MGIT broth tubes. This compound is sensitive to the presence of oxygen dissolved in the broth. Initially, the large amount of dissolved oxygen quenches the emissions from the compound and little fluorescence can be detected. Later, actively respiring microorganisms consume the oxygen and allow the fluorescence to be detected. The MGIT 960 system monitors the tubes for increasing fluorescence. Analysis of the fluorescence is used to determine if the tube is instrument positive, that is, the test sample contains viable organisms. Culture tubes which remain negative for a minimum of 42 days (up to 56 days) and which show no visible signs of positivity are removed from the instrument as negatives.

The principle of Xpert MTB/RIF assay is based on heminested real-time PCR. The sample was treated as per the instructions from the manufacturer. The test simultaneously detects MTB complex and resistance to rifampin in less than 2 hours.

The samples were also subjected to TB PCR targeting MPT 64 gene. DNA was extracted using heat lysis and chloroform. DNA obtained was amplified using gene-specific primer, Taq polymerase and deoxynucleotide triphosphates.

Statistical Analysis

Stata 14.0 software was used for statistical analysis. The *p*-value calculation was done by Pearson's chi-square test. Statistical significance was defined as *p*-value <0.05.

Results

Total 231,283 malignancies were diagnosed from January 1, 2019, to December 31, 2022, out of which 42 (prevalence 0.01816%) tested positive for TB. Yearwise distribution of total number of cases and TB-positive cases is shown in ►Fig. 1. Maximum number of samples were received in 2021. Twenty-eight samples were pulmonary, and the rest were extrapulmonary.

The samples were tested using ZN staining, GeneXpert, PCR, and MGIT. Testwise sample distribution and result obtained by the techniques are given in ►Table 2. Seven samples (1.37%) tested positive in ZN staining, 10 patients (6%) had culture positive by MGIT, 20 (10.53%) and 5 (13.51%) samples were positive by GeneXpert and PCR, respectively.

Of the 906 samples, 576 were males and 330 were females. Male:female ratio was 1.75:1. Genderwise result is shown in ►Table 3. Incidence of TB was more common among female cancer patients than male cancer patients, but the difference was statistically insignificant (*p*-value = 0.592).

Age range of patients was 2 to 85 years. Mean age was 47 years. Mean age of the TB-positive cases was 43 years, while mean age of the TB-negative cases was 47 years (*p*-value = 0.2142). Six (14%) of the TB-positive patients were children.

Table 2 Testwise sample distribution and result obtained

Method	Total tests	Number of positive cases (%)
GeneXpert	190	20 (10.53%)
MGIT	168	10 (6%)
PCR	37	5 (13.51%)
ZN	511	7 (1.37%)
Total	906	42

Abbreviations: PCR, polymerase chain reaction; ZN, Ziehl–Neelsen.

Table 3 Genderwise result of the test samples

Sex	Positive (%)	Negative (%)	Total
Female	17 (5.2)	313 (94.8)	330
Male	25 (4.3)	551 (95.7)	576
Total	42 (4.6)	864 (95.4)	906

Table 4 Percentagewise distribution of the 42 cancer patients who tested positive for TB

Type of cancer	% of cases	Number died (%)
Carcinoma lung	28	–
Leukemia	25	3 (30%)
Gastrointestinal cancer	13	–
Genitourinary cancer	13	1 (20%)
Hodgkin's lymphoma	9	3 (75%)
Carcinoma larynx	3	–
Carcinoma right breast	3	–
Malignant spindle cell tumor (leiomyosarcoma)	3	–
Squamous cell carcinoma	3	–
Total	100	7

Abbreviation: TB, tuberculosis.

Most (82%) of the patients were from north India (Delhi, Haryana, Uttar Pradesh, and Uttarakhand).

Percentagewise distribution of the 42 cancer patients who tested positive for TB is given in ►Table 4. Maximum number of TB-positive patients were found to be suffering from carcinoma lung (28%) followed by leukemia (25%), gastrointestinal cancer (13%), and genitourinary cancer (13%), respectively. Seven of the 42 patients succumbed to the disease; the cases belonged to Hodgkin's lymphoma (75% mortality), leukemia (30% mortality), and genitourinary (20% mortality).

Discussion

In this study, it is observed that samples tested across the defined period vary by wide margins. This may be due to the reason that during COVID-19 period, few samples were received. Hence in 2019 and 2020, fewer samples were received than in 2021 and 2022.

In this study, male:female ratio was 1.75:1. However, incidence of TB was more common among female cancer patients than male cancer patients, though the difference was statistically insignificant (p-value = 0.592). Contradictory findings have been reported by Nanthanangkul et al.[20]

In this study, maximum number (28%) of TB-positive patients were suffering from lung cancer. Similar findings have been reported in other studies as well.[1,13,20,24] Smoking may be a confounding factor for TB development in patients with lung cancer.[1] Moreover, misdiagnosis is possible due to mimic finding on the chest. The first case of coexistent TB and lung cancer was reported by Bayle in 1810.[25–27] Lung inflammation and fibrosis from TB can induce genetic damage, which may increase the risk of lung cancer.[28] Reverse causation is also possible, as occult lung cancer may cause TB infection and induce reactivation of latent TB by weakening the local immunity.[24] The regulatory T cells (Tregs) play an important role in this inhibition of immune response.[29] Tregs are characterized by presence of forkhead box P3 (Foxp3) molecule.[29] The high expression of Foxp3 was found in lung cancer cells and in tumor-infiltrating lymphocytes (TILs).[29] Cytotoxic T-lymphocyte antigen 4 (CTLA4) is constitutively expressed on Tregs and suppresses T cell activation.[29] Elevated CTLA4 expression in lymphocytes in patients with lung cancer has been found.[29]

In this study, leukemia was associated with the second highest risk of TB development among the investigated cancers. Similar findings have been reported in other studies as well.[1,30] Not only the disease itself but also the vigorous chemotherapy or aggressive therapeutic methods used to suppress the immune system in hematological cancer patients may lead to TB in these patients.[20,24] A predominance of Th2 lymphocytes, reduced percentages of T lymphocyte with costimulatory molecule expression, and impaired monocyte function play major roles in impaired immunity in leukemia.[31] Neoplastic cells can produce immunosuppressive cytokines and have low expressions of costimulatory molecules.[31]

In this study, gastrointestinal cancers also had considerable risk of TB (14%). Similar findings have been reported by other studies.[10,20] Numerous studies from Taiwan and Korea have also identified gastric cancer as an important risk factor for TB.[20,32,33] Since the digestive organs are important for nutrition, digestive organ dysfunction can lead to malnutrition and opportunistic infections.[20] Macrophages are a major component of TILs in gastrointestinal cancers.[34] Tumor-associated macrophages play a critical role in angiogenesis, metastasis, and immunosuppression.[34]

In this study, genitourinary cancers also had considerable risk of development of TB (14%). Similar findings have been reported by studies conducted by Nanthanangkul et al and Wu et al.[20,24]

In our study, mortality was highest (75%) in Hodgkin's lymphoma cases. For lymphoma, it is likely that TB infection affected bone marrow suppression.[20] A primary malignancy such as Hodgkin's lymphoma may cause a suppression of the cell-mediated immunity which predisposes to associated TB infection.[35–37] Several studies have reported that lymphomas are at an increased risk of the development of active TB.[18,38] Misdiagnosis or delay in diagnosis of both TB and Hodgkin's disease may occur because of identical signs and symptoms such as fever, cough, night sweats, loss of appetite, loss of weight, hepatosplenomegaly, and mediastinal adenopathy.[35] Immunosuppression is the main cause of TB in Hodgkin's disease and TB is the main cause of mortality in such cases.[35] Mycobacterial infections may lead to chronic persistent inflammatory process.[39] There is enough evidence that MTB can induce damage to cellular DNA involved in inflammatory carcinogenesis.[39] The pathogenesis hypothesized is that mycobacterial tuberculous infection causes direct DNA

damage and apoptosis inhibition, which increase mutagenesis of progeny cells, combined with angiogenesis favoring tumorigenesis.[35] Specifically, various mycobacterial cell wall components are hypothesized to induce the production of nitric oxide and reactive oxygen species which are involved in mutagenesis.[35] It may also be noted that both nitrative-DNA damage and oxidative-DNA damage have been implicated in inflammation-related carcinogenesis.[35]

A diagnosis of active TB affects the treatment administered to a cancer patient.[1] For example, chemotherapy or surgery may be delayed due to a TB diagnosis or accompanying medication therapy. In a study by Nair et al, 11% of cancer patients had to be changed from curative treatment to palliative treatment or no further treatment, TB being either the direct or indirect cause in all of them.[19] In another study by Ahn et al, the identification of TB infection interrupted the administration of bortezomib in patients with multiple myeloma, which significantly affected patient outcomes.[1,40] LTBI screening at the time of diagnosis of a high TB risk cancer may prevent the development of active TB during cancer treatment and enable the suitable administration of chemotherapy.[1]

Immunotherapy is used to treat many different types of cancer.[41] MTB reactivation may represent a direct complication of immunotherapy.[41] The management of MTB among cancer patients receiving immune checkpoint blockade–based cancer immunotherapy presents challenges.[41] Apart from the well-established clinical benefits of immunotherapy, the blockade of programmed death-1 (PD-1)/PD-1 ligand 1 (PD-L1) axis may simultaneously disturb the immune control of specific opportunistic infections such as TB which should be carefully managed in order to avoid compromising the result of cancer treatment and the patient's survival.[41] The prompt diagnosis of a mycobacterial infection, even in a subclinical stage, is crucial to avoid later aggravation.[41] Hence, screening for LTBI is suggested before initiation of an immunological checkpoint inhibitor (ICPI), especially in cancer patients with additional independent risk factors.[41] However, no available data exist for the management of latent or active TB during PD-1/PD-L1 blockade.[41] In general, in case of active TB, ICPIs are temporarily withheld and anti-TB treatment is timely initiated.[41] It has been suggested that 2 to 4 weeks after corresponding anti-TB treatment, ICPIs should be safely restarted or initiated.[41]

Developments in chemotherapeutic drugs and treatment modalities for cancer patients have led to rise in life expectancies.[1] It is important to identify patients at a high risk of developing active TB and provide appropriate treatment.[1] Cancer patients with decreased cellular immunity face an increased risk of active TB and remain in a prolonged state of immunocompromise.[1] Therefore, LTBI screening is needed to prevent opportunistic infection and should be performed at the time of cancer diagnosis, such as LTBI screening is performed at the time of human immunodeficiency virus diagnosis in developing countries.[1]

This study had a few limitations. First, it was performed retrospectively at a single center, and therefore, the results may not reflect the general population in India. Moreover, risk of active TB in cancer patients depends to large extent on epidemiological situation of TB in a certain geographic region. Hence, the results of this study should be carefully analyzed in countries with low TB incidence. The second shortcoming was that other factors such as the disease stage at the time of cancer diagnosis, chemotherapy, surgery, and radiotherapy were not included in the analysis.

Conclusion

In conclusion, the incidence of active TB is high in cancer patients, especially lung cancer, leukemia, gastrointestinal, and genitourinary cancers. Mortality was high in Hodgkin's lymphoma patients who developed TB. Therefore, we recommend targeted screening for TB in patients at the time of diagnosis of these high-risk cancers, followed by periodic screening. However, more studies need to be conducted from different regions to arrive at a conclusion.

Submission Statement

The material is original research, has not been previously published, and has not been submitted for publication elsewhere while under consideration.

Funding

None.

Conflict of Interest

None declared.

References

1 Cheon J, Kim C, Park EJ, et al. Active tuberculosis risk associated with malignancies: an 18-year retrospective cohort study in Korea. J Thorac Dis 2020;12(09):4950–4959
2 Taylor Z, Nolan CM, Blumberg HMAmerican Thoracic Society Centers for Disease Control and Prevention Infectious Diseases Society of America. Controlling tuberculosis in the United States: recommendations from the American thoracic society, CDC, and the Infectious Diseases Society of America. MMWR Recomm Rep 2005;54(RR-12):1–81
3 Snider DE Jr, Caras GJ, Koplan JP. Preventive therapy with isoniazid. Cost-effectiveness of different durations of therapy. JAMA 1986;255(12):1579–1583
4 Lecoeur HF, Truffot-Pernot C, Grosset JH. Experimental short-course preventive therapy of tuberculosis with rifampin and pyrazinamide. Am Rev Respir Dis 1989;140(05):1189–1193
5 Tuberculosis: NICE guideline. 2016. Available August 1, 2023 at: https://www.nice.org.uk/guidance/ng33
6 Canadian Tuberculosis Standards. 7th ed. Ottawa: Public Health Agency of Canada; 2014
7 Guidelines on the Management of Latent Tuberculosis Infection. Geneva: World Health Organization; 2015
8 Korean Guidelines for Tuberculosis. Joint Committee for the Revision of Korean Guidelines for Tuberculosis. 3rd ed. Cheongju: Korea Centers for Disease Control and Prevention; 2017
9 O'Garra A, Redford PS, McNab FW, Bloom CI, Wilkinson RJ, Berry MPR. The immune response in tuberculosis. Annu Rev Immunol 2013;31:475–527
10 Kim HR, Hwang SS, Ro YK, et al. Solid-organ malignancy as a risk factor for tuberculosis. Respirology 2008;13(03):413–419
11 Vynnycky E, Fine PE. The natural history of tuberculosis: the implications of age-dependent risks of disease and the role of reinfection. Epidemiol Infect 1997;119(02):183–201

12 Kiazyk S, Ball TB. Latent tuberculosis infection: an overview. Can Commun Dis Rep 2017;43(3-4):62–66
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(02): 1700157
14 De La Rosa GR, Jacobson KL, Rolston KV, Raad II, Kontoyiannis DP, Safdar A. *Mycobacterium tuberculosis* at a comprehensive cancer centre: active disease in patients with underlying malignancy during 1990-2000. Clin Microbiol Infect 2004;10(08):749–752
15 Kamboj M, Sepkowitz KA. The risk of tuberculosis in patients with cancer. Clin Infect Dis 2006;42(11):1592–1595
16 Latent Tuberculosis Infection: Updated and Consolidated Guidelines for Programmatic Management. Geneva: World Health Organization; 2018. Licence: CC BY-NC-SA 3.0 IGO
17 Getahun H, Matteelli A, Abubakar I, et al. Management of latent *Mycobacterium tuberculosis* infection: WHO guidelines for low tuberculosis burden countries. Eur Respir J 2015;46(06): 1563–1576
18 Cheng MP, Abou Chakra CN, Yansouni CP, et al. Risk of active tuberculosis in patients with cancer: a systematic review and meta-analysis. Clin Infect Dis 2017;64(05):635–644
19 Nair CK, Avaronnan M, Shenoy PK, et al. Impact of active tuberculosis on treatment decisions in cancer. Curr Probl Cancer 2021;45 (02):100643
20 Nanthanangkul S, Promthet S, Suwanrungruang K, Santong C, Vatanasapt P. Incidence of and risk factors for tuberculosis among cancer patients in endemic area: a regional cohort study. Asian Pac J Cancer Prev 2020;21(09):2715–2721
21 Shu CC, Liao KM, Chen YC, Wang JJ, Ho CH. The burdens of tuberculosis on patients with malignancy: incidence, mortality and relapse. Sci Rep 2019;9(01):11901
22 Kent PT, Kubica GP, eds. Public Health Mycobacteriology: A Guide for the Level III Laboratory. Atlanta, GA: Centers for Disease Control; 1985
23 Report AS. TB India 2020. RNTCP. Central TB Division, DGHS. Ministry of Health & Family Welfare. Accessed November 14, 2020, at: https://tbcindia.gov.in/
24 Wu CY, Hu HY, Pu CY, et al. Aerodigestive tract, lung and haematological cancers are risk factors for tuberculosis: an 8-year population-based study. Int J Tuberc Lung Dis 2011;15(01): 125–130
25 Bayle GL. Recherches sur la phthisie pulmonaire: Ouvrage lu à la Société de la faculté de médecine de Paris, dans diverses séances, en 1809 et. 1810. Gabon, French
26 Singh VK, Chandra S, Kumar S, Pangtey G, Mohan A, Guleria R. A common medical error: lung cancer misdiagnosed as sputum negative tuberculosis. Asian Pac J Cancer Prev 2009;10(03): 335–338
27 Christopoulos A, Saif MW, Sarris EG, Syrigos KN. Epidemiology of active tuberculosis in lung cancer patients: a systematic review. Clin Respir J 2014;8(04):375–381
28 Liang HY, Li XL, Yu XS, et al. Facts and fiction of the relationship between preexisting tuberculosis and lung cancer risk: a systematic review. Int J Cancer 2009;125(12):2936–2944
29 Domagala-Kulawik J, Osinska I, Hoser G. Mechanisms of immune response regulation in lung cancer. Transl Lung Cancer Res 2014;3 (01):15–22
30 Anibarro L, Pena A. Tuberculosis in patients with haematological malignancies. Mediterr J Hematol Infect Dis 2014;6(01):e2014026
31 Luczyński W, Krawczuk-Rybak M. [Mechanisms of immunosuppression in leukemia]. Postepy Hig Med Dosw 2005;59:28–33
32 Fang WL, Hung YP, Liu CJ, et al. Incidence of and risk factors for tuberculosis (TB) in gastric cancer patients in an area endemic for TB: a nationwide population-based matched cohort study. Medicine (Baltimore) 2015;94(47):e2163
33 Jung IY, Kim MH, Jeong WY, et al. Treatment outcomes of patients treated for pulmonary tuberculosis after undergoing gastrectomy. Tohoku J Exp Med 2016;240(04):281–286
34 Ma ES, Wang ZX, Zhu MQ, Zhao J. Immune evasion mechanisms and therapeutic strategies in gastric cancer. World J Gastrointest Oncol 2022;14(01):216–229
35 Reddy RC, Mathew M, Parameswaran A, Narasimhan R. A case of concomitant Hodgkin's lymphoma with tuberculosis. Lung India 2014;31(01):59–62
36 Poppema S. Immunobiology and pathophysiology of Hodgkin lymphomas. Hematology (Am Soc Hematol Educ Program) 2005;•••:231–238
37 Karakas Z, Agaoglu L, Taravari B, et al. Pulmonary tuberculosis in children with Hodgkin's lymphoma. Hematol J 2003;4(01):78–81
38 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 (03):720–725
39 Valchev D, Mitev M, Obretenov E, Kostadinov D, Petrov D. A combination of hodgkin's lymphoma and tuberculosis occurred with bilateral malignant pleural effusions. Ann Case Rep 2018; 2018(03):ACRT-169
40 Ahn JS, Rew SY, Yang DH, et al. Poor prognostic significance of *Mycobacterium tuberculosis* infection during bortezomib-containing chemotherapy in patients with multiple myeloma. Blood Res 2013;48(01):35–39
41 Anastasopoulou A, Ziogas DC, Samarkos M, Kirkwood JM, Gogas H. Reactivation of tuberculosis in cancer patients following administration of immune checkpoint inhibitors: current evidence and clinical practice recommendations. J Immunother Cancer 2019;7 (01):239

