IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

A Study of Radiological Presentation of Pulmonary Tuberculosis Among Diabetic Patients

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Abstract: Background: Several Asian nations are more severely impacted by the dual burden of diabetes mellitus (DM) and tuberculosis (TB) than other regions. According to a global estimate, DM may be responsible for 15% of all TB cases, with 40% of those cases coming from China and India. The second-leading cause of death in the global population, behind HIV/AIDS, is tuberculosis, according to the WHO. With their high rates of TB, predicted increases in DM incidence, and size of populations, many additional South, East, and South-East Asian nations are a cause for concern. Many other countries of South, East, and South-East Asia are of particular concern given their TB burdens, large projected increases in DM prevalence, and population size.
Objective: To evaluate the impact of glycemic status on radiological findings of PTB in diabetic patients.
Method: Between January 2022 and December 2022 chest radiographs (CXRs) in consecutive 40 DM patients with culture proved PTB were enrolled. An equal number of non-DM patients with similar demographics was included as the control group. Glycemic status was assessed by glycosylated hemoglobin (HbA1c), and a cutoff of 7% was used to further investigate radiological features of diabetic PTB. One radiologist and one pulmonologist reviewed the chest images independently.
Results: Compared with non-DM patients, primary PTB pattern and extensive disease on CXRs as well as primary PTB pattern, large area of heterogeneous lesion, more than one cavity in a single lesion, unusual location, and all lobe involvement of lesions CXRs were more common in DM patients. Furthermore, diabetics with HbA1c > 7% were more likely to exhibit unusual findings.
Conclusion: Diabetes-related PTB's radiographic symptoms were impacted by glycemic status. Physicians should be vigilant and pay more attention to patients with poor glycemic control given the increased likelihood of atypical radiological manifestations of PTB in DM patients.

1. INTRODUCTION

Both tuberculosis (TB) and diabetes mellitus (DM) are major global health concerns. Furthermore, the link between TB and DM has been established, and these conditions may worsen each other on multiple levels [1]. With the rising prevalence of tuberculosis (TB), particularly multidrug-resistant TB (MDR-TB), and diabetes cases worldwide in recent decades, the relationship has resurfaced as a major public health issue. Diabetes and tuberculosis are more closely linked in developing countries where tuberculosis is endemic, and the prevalence of DM is steadily increasing. In recent years, the global prevalence of tuberculosis has increased. In 2010, an estimated 8.8 million (range: 8.5-9.2 million) new cases of tuberculosis were diagnosed. Each year, approximately two million people are killed by tuberculosis. [2]. One reason for these findings is that diabetes patients' dysglycemia may impair their innate immune system, thereby producing an optimal habitat for tuberculosis. Intracellular bacterial infections are one of the most common diabetic consequences (e.g., tuberculosis). Dysglycemia may play a role in the link between diabetes and TB. [3]. M. tuberculosis is an aerobic, nonmotile rod that is resistant to drying, acid, and alcohol. It is primarily distributed through coughing and is passed from person to person via droplet nuclei holding the organism. A individual with active but untreated TB infects roughly 10-15 other persons each year. The quantity of infected droplets expelled by a carrier, the period of exposure, and M. tuberculosis virulence all influence the likelihood of transmission from one person to another. Individuals with compromised host cellular immunity, such as advanced age, malnutrition, cancer, immunosuppressive medication, HIV infection, end-stage renal disease, and diabetes, are more likely to acquire active TB [4]. Although the lower lung field may be involved on occasion, post-primary tuberculosis is usually found in the upper lung field. Lower lung field tuberculosis is a major source of concern in areas with a high tuberculosis burden. It frequently manifests as pneumonia, bronchiectasis, or bronchogenic carcinoma to avoid a proper diagnosis. Cases of middle and lower lung field tuberculosis have increased as a result of the current AIDS/HIV epidemic. [5]. The goal of this study is to provide more information on how tuberculosis manifests itself radiologically in the diabetic population.

2. MATERIALS AND METHODS

This study was conducted at Department of Pulmonary Medicine, Guru Gobind Singh Medical College and Hospital, Faridkot, India. It is a tertiary care teaching hospital. The study was a descriptive one that lasted a year, from January 2022 to January 2023. The college's ethical committee granted ethical clearance. The study included all patients with pulmonary tuberculosis. Inclusion and exclusion criteria were used to select patients with pulmonary tuberculosis and Diabetes mellitus (DMTB) and pulmonary tuberculosis without Diabetes mellitus (PTB). Before patients were included in the study, their consent was obtained. History was taken in full detail regarding particulars of the patient and complaints including cough, fever, hemoptysis, weight loss and anorexia, and history of contact with tuberculosis and history of any other systemic illness, diabetes mellitus, chronic liver diseases, asthma, chronic renal failure, and HIV were noted as well. Any relevant past history and personal history including dietary habits, smoking, alcohol, and other addictions were also taken. Diagnosis of tuberculosis was made by sputum for AFB examination by auramine-rhodamine stain (AR) technique and grading done accordingly using NTEP guidelines. Microbiological confirmed cases on CBNAAT (Cartridge-based nucleic acid amplification test) were taken in the study.
On a chest X-ray, lower lung field tuberculosis was defined as the area lying below the horizontal arbitrary line drawn across the hila (PA film). In the lower lung fields, the para hilar region was considered [6]. When lateral films were obtained, the disease was found in the lower lobes. The radiological reading was also recorded in terms of consolidation, nodular opacity, cavitation, and heterogeneous opacity. Recording of the abnormal shadows on chest X-ray includes the location using standard chest skiagram PA and lateral views; the extent of disease was classified as follows [7]:

Minimally advanced: lesion which was slight to moderate in density with no demonstrable cavitation, the total volume of lung on one side, present above the second chondrosternal junction, and spine of the fourth thoracic vertebra and no demonstrable cavity present (Figure 1).

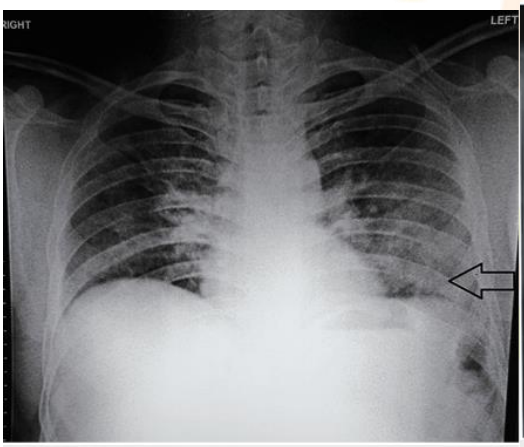

FIGURE 1: Chest X-ray with minimally advanced lesion.

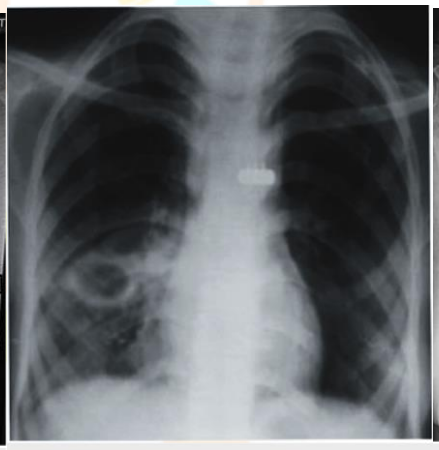
FIGURE 2: Chest X-ray showing moderately advanced lesion with cavity less than 4 cm in diameter.


FIGURE 3: Chest X-ray showing far advanced lesion with cavity more than 4 cm in diameter.

Moderately advanced: disseminated lesions of slight to moderate density that may extend throughout the total volume of one lung or the equivalent in both lungs; dense or confluent lesions are limited in extent to one-third of the volume of one lung; and total diameter of cavitations, if present, must be less than 4 cm (Figure 2).
Far advanced: lesion more extensive than moderately advanced one (Figure 3).
Patients with the following characteristics were excluded from the study: Patients less than 15 years of age were excluded, Patients who were Retro positive (HIV), Pregnant females and patient on immunomodulators, Organ transplant patients were excluded.
Diagnosis of diabetes was made according to WHO guidelines, that is, fasting plasma glucose $\geq$ 7.0 mmol/L (126 mg/dL) or 2 h plasma glucose $\geq$11.1 mmol/L (200 mg/dL). Strict control of sugar level was made during the treatment period. Patients were tested for HIV1 and HIV2 according to NACO guidelines [8]. Prolonged steroid intake was defined as steroid intake for more than three months

3. RESULTS

The total of 80 cases of pulmonary tuberculosis was studied. Among them 26 (32.5%) cases of patients were diagnosed as the case of lower lung field tuberculosis. Among lower lung field tuberculosis (LLFTB) 58 patients (72.5%) were males and 22 (27.5%) were females (Table 1). Mean age of patients in DMTB (Group A) was 53.25± 13.07years (15-70 years). The mean age of patients in PTB without DM was 35.03± 14.36 years (15-70 years). Most common clinical feature in Group A was fever (100%) followed by cough (95%), sputum (85%), and weight loss (82.5%), while in Group B most common clinical feature was both cough (97.5%) and fever (97.5%) followed by sputum (92.5%), and weight loss (90%). Group B patients presented significantly more with, fever, sputum and weight loss. However, there was significantly low occurrence of hemoptysis and loss of appetite as compared to Group B patients. (Table 2).

Table 1: Distribution of study participants based on gender

GENDER	GROUP A		GROUP B	
	NO.	%AGE	NO.	%AGE
MALE	27	67.5%	31	77.5%
FEMALE	13	32.5%	9	22.5%
TOTAL	40	100%	40	100%

In above mentioned table Higher male (72.5%) predominance was seen as compared to females (27.5%).

Table 2: Distribution of DMTB and PTB patients based on clinical presentation

CLINICAL PRESENTATION	GROUP A		GROUP B		P VALUE
FEVER	38	(95%)	39	97.5%	0.556
COUGH	40	(100%)	39	97.5%	0.314
SPUTUM	34	(85%)	37	92.5%	0.288
HEMOPTYSIS	6	(15%)	4	10%	0.499
LOSS OF WEIGHT	33	(82.5%)	36	90%	0.330
LOSS OF APETITE	34	(85%)	35	87.5%	0.745

Majority of the participants in both groups presented commonly with Fever, Cough and sputum production.

Mean random blood sugar (251+ 94.29 mg/dl) and HBA1C (10.4+ 1.8 %) was found to be significantly higher in Group A as compared to mean random blood sugar (95.50+ 15.64 mg/dl) and HBA1C (4.9+ 0.3 %) in Group B ($P<0.05$). All other laboratory parameters were not found to be statistically significant ($P>0.05$) (Table 3).

Table 3: Comparison of laboratory parameters of study participants

PARAMETER	GROUP A	GROUP B	P VALUE
HEMOGLOBIN (g/dl)	10.50 ± 1.64	9.66 ± 1.56	0.329
RANDOM BLOOD SUGAR (mg%)	251.95 ± 94.28	95.50 ± 15.64	<0.0001
HBA1C (%)	10.4 ± 1.8	4.9 ± 0.3	<0.0001

Upon statistical analysis, mean random blood sugar and HBA1C was found to be significantly higher in Group A as compared to Group B ($P<0.05$).

The distribution of lung lesions (Heterogeneous and Cavity lesion) based on location on chest x-ray between Group A and Group B was found to be statistically significant ($p<0.05$). Group A showed higher lower lung field involvement 27.5% as compared to Group B. While group B showed upper lung field involvement 37.5% (Table 4).

Table 4: Distribution of lung lesions based on location on chest x-ray

NO.	CHEST X RAY ZONES	GROUP A		GROUP B		P-VALUE
		NO.	%AGE	NO.	%AGE	
1.	UPPER ZONE	0	0%	15	37.5%	<0.0001
2.	MID ZONE	4	10%	3	7.5%	
3.	LOWER ZONE	10	25%	0	0%	
4.	UPPER + MID ZONE	4	10%	13	32.5%	
5.	MID + LOWER ZONE	16	40%	4	10%	
6.	UPPER +MID +LOWER ZONE	6	15%	5	12.5%	
TOTAL		40	100%	40	100%	

The above table shows distribution of study participants based on involvement of zone on chest x-ray. This was found to be statistically significant ($p<0.05$), meaning that Diabetic group of TB patients had higher lower lung zone tuberculosis while non-diabetic group showed the opposite.

In Group A, 60% participants showed moderate disease, followed by 22.5% participants had far advanced disease and 17.5% participants had minimal disease. In Group B, 42.5% participants showed moderate disease, followed by 35% participants had far advanced disease and 22.5% participants had minimal disease (Table 5). The distribution of study participants based on diagnosis between two groups was not found to be statistically significant ($p>0.05$).

Table 5: Distribution of study participants based on radiological diagnosis

DIAGNOSIS	GROUP A		GROUP B		P VALUE
	NO.	%AGE	NO.	%AGE	
MINIMAL	5	12.5%	9	22.5%	0.669
MODERATE	19	47.5%	23	57.5%	
FAR ADVANCED	16	40%	16	40%	
TOTAL	40	100%	40	100%	

Majority of the patients from Group A and Group B belong to Moderately advanced disease group followed by Far advanced disease group according to the radiological classification mentioned by Crofton and Douglas in 5th edition of respiratory diseases book.

DISCUSSION

Diabetes is a debilitating disease that impairs the cellular immune system and provides the ground for TB. The leukocyte dysfunction and reduction of serum bactericidal activity in DM patients increases the risk of TB infection. Prompt and appropriate treatment is the most effective way to prevent treatment failure, relapse, or emergence of multi drug resistant TB (MDR-TB) which are the main constraints in fighting against TB. Because of the differences in the immune system response of diabetics and non-diabetic infected hosts, epidemiological, clinical, radiological, laboratory tests results and response to treatment may vary in these patients [9,10].

In the present study, the mean age of participants in Group A and Group B was 53.25 ± 13.07 and 35.03 ± 14.36 years respectively. The mean age was higher in Group A as compared to Group B. This is in accordance with the findings of Alavi SM et al [11], who observed in their study that mean age in the DM & PTB and Non-DM & PTB group was 56.6 ± 12.7 was 44.8 ± 18.3 years respectively. Ezung T et al [12] have also shown that the mean age of TB patients with diabetes is higher than non-diabetic TB patients. The prevalence of higher mean age in diabetics as compared to non-diabetics can be attributed to the fact that old TB infected persons are at increased risk of TB reactivation; secondly, the incidence of diabetes is higher in the older age. The study population showed male predominance. There were 67.5% males and 32.5% females in Group A. Group B included 77.5% males and 22.5% females. Male preponderance was also seen in studies by Bokam DBR [13] and Goganti S et al [14].

The findings of Alavi SM et al [11] revealed that cough, fever and night sweats in diabetic patients are the same in non-diabetic patients, but the sputum production, hemoptysis, and dyspnea are observed in the diabetics more frequent than in non-diabetics. Baghaei P et al [15] has demonstrated that anorexia, dyspnea and hemoptysis in diabetes were higher than in non-diabetes but, cough and sputum production in both groups were similar. The distribution of study participants based on any clinical presentation between two groups was not found to be statistically significant in our study ($p>0.05$). Mean random blood sugar and HBA1C was found to be significantly higher in Group A as compared to Group B ($P<0.05$). Sharma A et al [16] observed in their study that in tuberculosis, higher HbA1C and sugar levels are associated with more chest x-ray lesions. Hence, to obtain adequate control of DM and lower hospitalization, TB patients must have good glycemic control.

The distribution of study participants based on radiological features (cavity size and location of lung lesion) between two groups was found to be statistically significant ($p<0.05$). In study by Shaikh et al [17], the prevalence of cavitary lesions was comparable in those with and without diabetes. The PTB DM group had higher cavitary lesions that were restricted to lower lung field. In a study patient with diabetes experienced cavitations more frequently in the lower lung fields as compared to non-diabetic [18] which was comparable to our study. The proportion of typical presentations and cavitary lesions was higher in diabetic individuals on chest radiograph in study by Shiva et al [19], and there was discernible difference between the two groups in terms of radiological presentation. Mohapatra et al [20] observed that two groups differ in terms of radiographic localization of lung lesions or the presence of cavitation, lower lung field infiltration suggesting that the impact of diabetes on TB as compared to non-diabetic patient. However, Zhan S et al [21] observed that TB patients with hyperglycemia presented with cavities and alveolar infiltrates more frequently than those with normoglycemia. They inferred that over- expression of cytokines, such as CRP in TB-DM patients were associated with escalating neutrophil recruitment and infiltration, which led to more inflammation and necrosis, and then potentially resulted in cavity formation. Another mechanism contributing to the severe inflammation is adaptive immune dysfunction. Impaired T helper 1 cell lowers production of IFN-γ, which weaken the killing activity of macrophages and leads to failing control of mycobacterium growth [22]. High bacterial load and over inflammation in turn gives rise to development of more extensive lung lesions, cavitation and infiltration extending to more lobes [23].

Paralija et al [24] also concluded by their study that TB is more likely to manifest in diabetes patients as abnormal radiological pictures, and the pace of radiological TB infiltrate retreat is slower in diabetic patients. Shaikh et al [17] observed that diabetes was the significant risk factor for lung lesions or cavities in the lower lung fields and cavitary lesions and atypical radiological scans are more likely to be present in the PTB DM group. Alavi SM et al [11] reported that there is a similar frequency of infiltration and upper lobe opacity in both groups, but there is a higher frequency of the cavity lesions and reticulonodular pattern in diabetic patients comparing with non-diabetic patients.

CONCLUSION

Lower lung field tuberculosis is a fairly common entity among immunocompromised individuals. It can be confused with the more common pneumonias located at that location causing the undue diagnosis and delay in the treatment. It affects males more commonly as compared to females and tuberculosis should be looked in males with lower lung field lesions. It differs from upper lung field tuberculosis in clinical and radiological features which is seen among immunocompetent individuals. Cough and hemoptysis are the most frequent presentation of LLFTB as compared to non-LLFTB cases. Consolidation and cavitation are the most frequent finding on chest X-ray in LLFTB cases in comparison to infiltration seen in non-LLFTB cases. Patients with diabetes, HIV, and end stage renal disease cases and persons on corticosteroid frequently present with LLFTB. Short course antitubercular chemotherapy is quite an effective mode of treatment in treating LLFTB.

DISCLOSURES

Human subjects: Consent was obtained or waived by all participants in this study. Ethics Committee G.G.S Medical College and Hospital, Faridkot issued approval NA. Animal subjects: All authors have confirmed that this study did not involve animal subjects or tissue. Conflicts of interest: In compliance with the disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work

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REFERENCES

1. Huang, Li-Kuo: The Impact of Glycemic Status on Radiological Manifestations of Pulmonary Tuberculosis in Diabetic Patients.. PloS One, vol. 12, no. 6. 2017:179750. 10.1371/journal.pone.0179750

2. Baghaei, P., Marjani, M., Javanmard, P: Diabetes mellitus and tuberculosis facts and controversies. J Diabetes Metab Disord 12. 58:

3. Chen Z, Liu Q, Song R, et al.: The association of glycemic level and prevalence of tuberculosis: a meta- analysis. BMC Endocr Disord. 2021, 16:123-10. 10.1186/s12902-021-00779-6

4. Jeong, Yeon Joo, and Kyung Soo Lee: "Pulmonary Tuberculosis: Up-to-Date Imaging and Management." AJR. American Journal of Roentgenology, vol. 191, no. 3. 2008:834-844. 10.2214/AJR.07.3896

5. Singh, Saurabh Kumar, and Kamlesh Kumar Tiwari: Clinicoradiological Profile of Lower Lung Field Tuberculosis Cases among Young Adult and Elderly People in a Teaching Hospital of Madhya Pradesh, India. Journal of Tropical Medicine, vol. 20152015230720, 10.1155/2015/230720

6. Segarra, F., "Lower Lung Field Tuberculosis." The. American Review of Respiratory Disease, vol. 87, 1963, pp. 37-40. 10.1164/arrd.1963.87.1.37

7. Leitch, A. Gordon: Pulmonary Tuberculosis: Clinical Features. Crofton and Douglas's Respiratory Diseases, Blackwell Science Ltd. 2008, pp.:507-527. 10.1002/9780470695999.ch17

8. National AIDS Control Organization, Ministry of Health & Family Welfare, and Government of India, Antiretroviral Therapy Guidelines for HIV Infected Adults and Adolescents including Post-Exposure, National AIDS Control Organization, Ministry of Health & Family Welfare, Government of India, 2013. http://www.naco.gov.in/NACO/About_NACO/Policy Guidelines/Policies Guidelines1/.

9. Delamaire M, Maugendre D, Moreno M, Le Goff MC, Allannic H, Genetet B: Impaired leucocyte functions in diabetic patients. Diabet Med [Internet. 19972023, 9:29-34.

10. McMahon MM, Bistrian BR: Host defenses and susceptibility to infection in patients with diabetes mellitus [Internet]. Vol. 9. Infectious Disease Clinics of North America. 19952023, 9:1-9.

11. Alavi SM, Khoshkho MM, Salmanzadeh S, Eghtesad M: Comparison of epidemiological, clinical, laboratory and radiological features of hospitalized diabetic and non-diabetic patients with pulmonary tuberculosis at Razi hospital in Ahvaz. Jundishapur J Microbiol [Internet. 20142023879,

12. Ezung T, Devi NT, Singh NT, Singh TB: Pulmonary tuberculosis and diabetes mellitus--a study. J Indian Med Assoc. 2002, 100:376-378.

13. Bokam DBR: Effect of Glycemic Control on Radiographic Presntation of Pulmonary Tuberculosis in Type 2 Diabetes Mellitus. J Med Sci Clin Res. 2017, 10:5.

14. Goganti S, Kumari S L, Thomas A, Prasad B H, B R, C C. RADIOLOGICAL PATTERN OF PULMONARY TUBERCULOSIS IN DIABETICS VISITING A TERTIARY CARE HOSPITAL: J Evol Med Dent Sci. 2017, 23:5920-3. 10.14260/jemds/2017/1287

15. Baghaei P, Tabarsi P, Abrishami Z, Mirsaeidi M, Faghani YA, Mansouri SD: Comparison of Pulmonary TB Patients with and without Diabetes Mellitus Type II. Tanaffos. 2010, 9:13-20.

16. Sharma A, Vijapurkar S, Gosavi S, Samgamesh S, E A, Uttam R: Spectrum and Correlation of Clinical, Radiological and Biochemical Parameters in Tuberculosis in a Hospital in South India. J Evid Based Med Healthc [Internet. 20212023, 9:410-4. 10.18410/jebmh/2021/80

17. Shaikh MA, Singla R, Khan NB, Sharif NS, Saigh MO: Does diabetes alter the radiological presentation of pulmonary tuberculosis. Saudi Med J [Internet. 2003:278-81.

18. Pérez-Guzman C, Torres-Cruz A, Villarreal-Velarde H, Salazar-Lezama MA, Vargas MH: Atypical radiological images of pulmonary tuberculosis in 192 diabetic patients: a comparative study. The. International Journal of Tuberculosis and Lung Disease: the Official Journal of the International Union Against Tuberculosis and Lung Disease. 2001, 5:455-461.

19. (PDF) Comparison of pulmonary TB patients with and without diabetes mellitus Type II [Internet]. [cited. (202310). https://www.researchgate.net/publication/281870304_Comparison_of_pulmonary_TB_patients_with_and_without_diabetes_m

20. Mohapatra AK, Singh P, Subhankar S: Study of clinical and radiological profile of pulmonary tuberculosis among patients having diabetes mellitus. Int J Adv Med [Internet. 20172023, 9:4.

21. Zhan S, Juan X, Ren T, et al.: Extensive Radiological Manifestation in Patients with Diabetes and Pulmonary Tuberculosis: A Cross-Sectional Study. Ther Clin Risk Manag [Internet. 2022, 23:595-602. 10.2147/TCRM.S363328

22. Ayelign B, Negash M, Genetu M, Wondmagegn T, Shibabaw T: Immunological Impacts of Diabetes on the Susceptibility of Mycobacterium tuberculosis [Internet]. Vol. 2019, Journal of Immunology Research. 201920239. https://pubmed.ncbi.nlm.nih.gov/31583258/.

23. Orme IM, Robinson RT, Cooper AM: The balance between protective and pathogenic immune responses in the TB-infected lung. Nat Immunol. 2015, 16:57-63. 10.1038/ni.3048

24. Radiological features of pulmonary tuberculosis in patients with diabetes mellitus | European Respiratory Society [Internet]. [cited. (20238). https://erj.ersjournals.com/content/38/Suppl_55/p2607