CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.3334282

Available online at: http://www.iajps.com *Research Article*

CLINICAL FEATURES OF TUBERCULOSIS; A COMPARATIVE ANALYSIS OF ITS ASSOCIATION AMONG DIABETIC AND NON-DIABETIC PATIENTS

Mahnoor Khalil Ahmed[1], Baquar Raza[2], Kanwal Abbas Bhatti[3], Nusret Kharadi[4], Mamoona Sadia[5] and Yumna Ahmed[6]

Karachi Medical & Dental College, Abbasi Shaheed Hospital, Karachi[1, 2, 4 – 6]

Liaquat University of Medical & Health Sciences, Jamshoro[3]

Article Received: May 2019 **Accepted:** June 2019 **Published:** July 2019

Abstract:

Background: *Diabetes mellitus has in recent times revealed a shocking augmentation globally and there are increasing facts demonstrating that DM affects presentation and outcome of treatment in patient of TB disease.*

Objective*: To compare the presentations of complaints of patients of Pulmonary Tuberculosis with and without diabetes mellitus.*

Methodology: *This observational study was conducted on 107 pre-diagnosed patients of pulmonary tuberculosis through non probability convenient sampling from January 2014 to December 2015 in Medical unit 1, Abbasi Shaheed Hospital, Karachi after taking ethical approval. Patients with age between 20 to 70 years diagnosed with pulmonary tuberculosis were included in the study. Patients with multiple co-morbids, mass lesion on chest x-ray, smokers, with known respiratory illness, were excluded. Clinical features of patients were observed and recorded in diabetic and non diabetic group. Statistical analysis was done via help of SPSS v, 20.0.*

Results: *In total of 107 patients, mean age of patients with diabetes was 61.47± 12.57 while that of non diabetics was 40.49 ±14.49. The frequency of clinical features including shortness of breath, productive cough, chest pain, hemoptysis and effusion was higher in diabetics as compared to non diabetic tuberculosis patients with significant association ($p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$, $p=0.018$). Furthermore, patients in diabetic group, presented with renal failure in 32(80%) with significant association ($p<0.001$)*

Conclusion: *The features including shortness of breath, productive cough, chest pain, hemoptysis, pleural effusion and renal failure were observed to be more common in TBDM while night sweats, fever and fatigue in TBNDM group.*

Key Words: *Clinical features, Diabetic, non-diabetic and tuberculosis.*

Corresponding author:

Dr. Mahnoor Khalil Ahmed,

(MBBS, FCPS), Assistant Professor, Department of Medicine

Karachi Medical & Dental College, Abbasi Shaheed Hospital, Karachi

+92-336-3454788

QR code

Please cite this article in press Mahnoor Khalil Ahmed et al., ***Clinical Features Of Tuberculosis; A Comparative Analysis of its Association among Diabetic & Non-Diabetic Patients.,*** *Indo Am. J. P. Sci, 2019; 06(07).*

INTRODUCTION:

Tuberculosis (TB) is one of the leading transmissible diseases globally [1]. In the developing world it is a chief public health hazard [2]. Nowadays more TB cases are being observed than at any other time in history attributed to emerging multidrug-resistance (MDR) strains of TB, epidemics of human immunodeficiency virus (HIV), diabetes mellitus, malnutrition, air pollution, malignancies, drug abuse especially alcohol and smoking with increasing age [3-5]. A variety of clinical presentations in humans are due to infectivity with Mycobacterium tuberculosis, the causative organism of tuberculosis (TB).This bacterium typically attacks the lungs, however it can also harm other organs of human body including bones and intestine.

Majority of the infections are asymptomatic clinically, in a controlled state that is termed latent TB infection (LTBI); a lesser division of infected individuals manifests as symptomatic, active TB [6]. Sputum-negative pulmonary TB patients (PTB) and extra-pulmonary TB (EPTB) patients are difficulty to be diagnosed and may be left undiagnosed at any point of care. Since the presentation of TB may be similar those of other diseases like sarcoidosis and pulmonary neoplasms, that makes diagnostic imaging a challenge. An elevated point of pre-test clinical thought based on history is elementary in the diagnostic work-up of TB as clinical signs and symptoms in affected adults can be non-specific [7].

Characteristically, PTB can be alienated into a primary and a post-primary pattern, each can present with distinguishing radiological features. However, it is extremely complex to make a distinctive linein practice among these radiographic patterns and substantial overlaping can be observed in the radiological manifestations [8]. First-time contact to Mycobacterium tuberculosis leads to primary TB. At radiology, primary PTB manifests as four main entities – parenchymal disease, lymphadenopathy, pleural effusion, and miliary disease – or any combination of these [9]. Post-primary PTB is one of the numerous terms (including reactivation, secondary, or adulthood) given to the type of TB that develops and progresses under the influence of acquired immunity [8] .Post-primary PTB mostly manifests on radiography as focal or patchy heterogeneous, poorly defined consolidation that involves the apical and posterior segments of the upper lobes and the superior segments of the lower lobes [7].

In general, TB can be cured with antibiotics. Though, the organisms in patient with TB can become resistant to two or more of the standard drugs, which is the utmost catastrophe that can happen. In dissimilar to drug sensitive (DS) TB, its multi-drug resistant (MDR) appearance is additionally complicated and expensive to recover from. Therefore, timely recognition of the MDR category is elementary for an efficient management [10].

DM has in recent times revealed a shocking augmentation globally and there are increasing facts demonstrating that DM affects presentation and outcome of treatment in patient of TB disease [11,12] . Fundamentally, studies in animal models of diabetes and TB and prior vivo studies with immune cells from patients with diabetes propose a model where the preliminary *Mycobacterium tuberculosis* infection in the diabetic host is characterized by a delayed and low performing response by monocytes and macrophages. These defects offer a vital early chance for encouraging replication of *M. tuberculosis* within the diabetic alveolar macrophages [13]. Higher frequencies of certain clinical findings such as lower lung field lesions, cavities and acid-fast bacilli (AFB) smear positivity among patients with TB and DM (TBDM) comorbidity has been revealed by numerous studies [14,15]. It has been lately shown that patients with TBDM comorbidity from South India exhibit higher level of plasma biomarkers of inflammation, tissue remodeling, and oxidative stress; all of these could lead to increased susceptibility to worse TB-related clinical outcomes [16].

Nonetheless, no study to date has investigated the association of DM with clinical presentations of TB patients in Pakistan. Thus, this study was conducted to explore the role of DM on clinical presentations of newly diagnosed TB patients.

METHODOLOGY:

Cross sectional observational study through non probability convenient sampling technique was carried out for a period of two years from January 2014 to December 2015 in Medical unit 1, Abbasi Shaheed Hospital, Karachi. Ethical permission was taken from the Institutional review board of the hospital.

One hundred and seven In-patients who were diagnosed to have pulmonary tuberculosis were chosen for this study and were divided into two groups including diabetic and non diabetic. Patients with age between 20 to 70 years, new onset of respiratory symptoms, non smokers, not associated with acute illness, raised ADA level on pleural D/R,

chest radiographic findings of patchy infiltrates, bilateral or unilateral hilar lymphadenopathy, cavitations, homogenous patch & pleural effusion and known cases of diabetes mellitus with respiratory complaints were included in this study. Patients with multiple co-morbids, mass lesion on chest x-ray, smokers, with known respiratory illness, no positive sputum or pleural fluid findings and with extra pulmonary tuberculous symptoms were excluded. Informed consent was taken from the patients with complete concealment of the data. All patients were examine for respiratory symptoms and investigated with chest X-ray, Sputum studies, pleural fluid studies (D/R, C/S, Gene Expert and ADA levels), HbA1C and ultrasound kidney ureter and bladder. All investigations were done from Abbasi Shaheed hospital laboratory, Hopes laboratory and lab collection points of Ziauddin or Agha Khan University Hospital. All patients were started on Anti Tuberculous Therapy on the basis of radiographic findings, sputum studies, or pleural fluid studies and those who responded to the treatment within 3 weeks were taken as subjects.

Data analysis:

For analysis of data the statistical software SPSS version 20.0 was used. Quantitative data was presented as mean ± SD while qualitative was presented as frequency (%). T-test and chi- square test were used to assess the significance and p-value was set at 0.05.

.

Table 1: Comparison of quantitative variables in diabetic and non diabetic TB patients

	Diabetes		p-value
	Yes(n=40)	No(n=67)	
	Mean ± SD	Mean ± SD	
Age(years)	61.47±12.57	40.49±14.49	<0.001
Specific Gravity	0.95±0.32	0.52±0.52	<0.001
Lymphocytes (%)	69.61±9.44	76.66±10.54	0.005
Neutrophils (%)	28.11±9.40	21.33±13.26	0.016
LDH	821.05±460.77	368.95±470.64	<0.001
Proteins	6.50±2.13	3.24±3.48	<0.001
Creatinine Clearance	45.10±9.95	58.61±3.60	<0.001

Table 2: Association of clinical features in two groups

Variables (n=107)		Diabetes		p-value
		Yes(n=40)	No(n=67)	
		n(%)	n(%)	
Gender	**Male**	23 (57.5%)	39 (58.2%)	0.943
	Female	17 (42.5%)	28 (41.8%)	
Night Sweats	**Present**	6 (15.0%)	49 (73.1%)	<0.001
	Absent	34 (85.0%)	18 (26.9%)	
Fever	**Present**	12 (30.0%)	58 (86.6%)	<0.001
	Absent	28 (70.0%)	9 (13.4%)	
Fatigue	**Present**	27 (67.5%)	51 (76.1%)	0.332
	Absent	13 (32.5%)	16 (23.9%)	
Shortness of breath	**Present**	35 (87.5%)	23 (34.3%)	<0.001
	Absent	5 (12.5%)	44 (65.7%)	
Productive Cough	**Present**	38 (95.0%)	30 (44.8%)	<0.001
	Absent	2 (5.0%)	37 (55.2%)	
Chest Pain	**Present**	33 (82.5%)	22 (32.8%)	<0.001
	Absent	7 (17.5%)	45 (67.2%)	
Hemoptysis	**Present**	21 (52.5%)	7 (10.4%)	<0.001
	Absent	19 (47.5%)	60 (89.6%)	
Effusion	**Present**	25 (62.5%)	26 (38.8%)	0.018
	Absent	15 (37.5%)	41 (61.2%)	
Renal Failure	**Present)**	32 (80.0%)	9 (13.4)	<0.001
	Absent	8 (20.0%)	58 (86.6)	

RESULTS:

Total 107 diagnosed cases of tuberculosis were taken who were divided into 40 diabetic (23 males while 17 females) and 67 non diabetic (39 males while 28 females) patients. Mean age of patients with diabetes was 61.47± 12.57 while that of non diabetics was 40.49 ±14.49.Significant difference was observed in specific gravity, lymphocytes, neutrophils, LDL, proteins and creatinine levels in diabetic and non diabetic groups. (Table-1) Night sweat was present in

6(15.0%) patient with diabetes whereas it was present in 49(73.1%) patients without diabetes with significant difference (p<0.001).Fever was present in 12(30.0%) patient with diabetes whereas it was present in 58(86.6%) patients without diabetes with significant difference (p<0.001). Fatigue was present in 27(67.5%) patient with diabetes whereas it was present in 51(76.1%) patients without diabetes with insignificant difference (p=0.332).Shortness of breath was present in 35(87.5%) patient with diabetes whereas it was present in 23(34.3%) patients without diabetes with significant difference (p<0.001).Productive Cough was present in 38(95.0%) patient with diabetes whereas it was present in 30(44.8%) patients without diabetes with significant difference (p<0.001).Chest Pain was present in 33(82.5%) patient with diabetes whereas it was present in 22(32.8%) patients without diabetes with significant difference (p<0.001). Hemoptysis was present in 21(52.5%) patient with diabetes whereas it was present in 7(10.4%) patients without diabetes with significant difference (p<0.001).Effusion was present in 25(62.5%) patient with diabetes whereas it was present in 26(38.8%) patients without diabetes with significant difference (p=0.018). Renal Failure was present in 32 (80.0%) patient with diabetes whereas it was present in 9 (13.4%) patients without diabetes with significant difference (p<0.001). (Table-2)

DISCUSSION:

The study reported the significant differences in clinical presentation of TB patients with diabetes mellitus (TBDM) and without diabetes mellitus (TBNDM) in which shortness of breath, productive cough, chest pain, hemoptysis, pleural effusion and renal failure seen more in TBDM while night sweats, fever, fatigue in TBNDM group. This is consistent with the study conducted in Brazil that showed that diabetic individuals more frequently presented with cough, night sweats, hemoptysis and malaise than those without DM. Another study of Texas-Mexico revealed that TBDM group was more likely to have hemoptysis and pulmonary cavitation as compared to TBNDM group [17]. Similarly one more study done in Indonesia which revealed cough (86.4% in diabetes, 80.7% in non-diabetes),hemoptysis (12.4% in diabetes, 8.3% in non-diabetes), tiredness (11.4% in diabetes, 6.0% in non-diabetes) and weight loss (35.1% in diabetes, 22.1% in non-diabetes) [18] . Another study of Taiwan was consistent with our study in which cough (98.9% in TBDM, 97.8% in TBNDM), dyspnea (69.1% in TBDM, 63.7% in TBNDM), and hemoptysis (42.6% in TBDM, 40.7% in TBNDM) was revealed [19]. Several other studies done in Saudi Arabia [20], Turkey [22], Tehran–Iran [23] and Tanzania [24] contradict with our study in which no substantial difference was noted in symptoms of the two groups. According to a study conducted in Thailand, anorexia was observed considerably more commonly in PTB patients with DM, the presenting symptom of cough was seen notably more commonly in PTB patients without DM whereas prevalence of other presenting symptoms and signs, including dyspnea, fever, chest pain, hemoptysis were equal in both groups [21] which was comparable to those findings of a previously done study reporting that the clinical presentation of PTB differ slightly among patients with and without DM [24]. Furthermore one more study done by Workneh MH et al. revealed no significant difference of clinical presentations in aforementioned two groups [3].

This study has numerous strengths. To the best of our information, this is one of the small number of studies conducted in Pakistan and may be used as a baseline for upcoming superior studies. The qualitative approach of our study has assured that we have assessed the extensive range of patients with tuberculosis. However the study might not be immune from observer and selection bias. Considering the observations of our study and to what range these clinical features might be consistent with other co-morbids in patients would be helpful to discover more facts about the clinical features of tuberculosis.

CONCLUSION:

The present study revealed that a significant difference in clinical manifestations between TB patients with diabetes mellitus (TBDM) and without diabetes mellitus (TBNDM) exited in the patients. The features including shortness of breath, productive cough, chest pain, hemoptysis, pleural effusion and renal failure were observed to be more common in TBDM while night sweats, fever, fatigue in TBNDM group.

REFERENCES:

1. Abolo M benti L. Peritoneal tuberculosis, J cases of acute abdomen recently operated upon. J Chir-Paris.1991: 337-80.
2. Niazi AK, Kalra S. Diabetes and tuberculosis: a review of the role of optimal glycemic control. J Diabetes Metab Disord.2012;11:28.
3. Workneh MH, Bjune GA and Yimer SA. Diabetes mellitus is associated with increased mortality during tuberculosis treatment: a prospective cohort study among tuberculosis patients in South-Eastern Amahra Region, Ethiopia.Infectious Diseases of Poverty.

2016;5:22.
4. Das P, Horton R. Tuberculosis-time to accelerate progress. The Lancet. 2010; 375(9718):1755–57.
5. Lönnroth K, Jaramillo E, Williams BG, Dye C, Raviglione M. Drivers of tuberculosis epidemics: The role of risk factors and social determinants. SocSci Med. 2009; 68:2240–6.
6. MA, Fortune MS and Flynn JL. Heterogeneity in tuberculosis. Nature Reviews Immunology.2017;17:691–702.
7. SkouraaE, Zumla A, Bomanji J. Imaging in tuberculosis. Elsevier ltd on behalf of international journal for infectious diseases.2015;32:87-93.
8. Dyck PV, Vanhoenacker FM, Brande PV, Schepper AMD. Imaging of pulmonary tuberculosis.Eur Radiol.2003; 13:1771-1785.
9. Kaufmann SH, Rubin E, A. Zumla A. Clinical tuberculosis, Cold Spring Harbor Laboratory Press, New York.2014.
10. Dicente Cid, Y., Kalinovsky, A., Liauchuk, V., Kovalev, V., ,M¨uller, H. Overview of ImageCLEFtuberculosis 2017 - predicting tuberculosis type and drug resistances in CLEF 2017 Labs Working Notes. CEUR Workshop Proceedings, Dublin, Ireland, CEUR-WS.org (September 11-14 2017).
11. Dooely KE, Chaisson RE. Tuberculosis and diabetes mellitus: Convergence of two epidemics. Lancet Infect Dis. 2009;9(12):737–46.
12. Sen T, Joshi SR, Udwadia ZF. Tuberculosis and diabetes mellitus: Merging epidemics. J Assoc Physicians India. 2009;57:399–404.
13. Restrepo B.I. (2018) Diabetes and Tuberculosis. In: Venketaraman V. (eds) Understanding the Host Immune Response Against Mycobacterium tuberculosis Infection. Springer, Cham.2018:1-21.
14. Carreira S, Costeira J, Gomes C, André JM, Diogo N. Impact of diabetes on the presenting features of tuberculosis in hospitalized patients. Rev Port Pneumol. 2012;18(5):239–43
15. Shital P, Anil J, Sanjay M, Mukund P. Tuberculosis with diabetes mellitus: clinical-radiological overlap and delayed sputum conversion needs cautious evaluation-prospective cohort study in tertiary care hospital. India J PulmRespir Med. 2014;4:175.
16. Gil-Santana L, Almeida-Junior JL, Oliveira CAM, Hickson LS, Daltro C, Castro S, et al. Diabetes Is Associated with Worse Clinical Presentation in Tuberculosis Patients from Brazil: A Retrospective Cohort Study. PLoS ONE.2016;11(1):e0146876.
17. Restrepo BI, Fisher-Hoch SP, Crespo JG, Whitney E, Perza A, Smith B. Type 2 diabetes and tuberculosis in a dynamic bi-national border population. Epidemiol Infect. 2007;135(3):483–91.
18. Chiang CY, Bai KJ, Lin HH, Chien ST, Lee JJ, Enarson DA, et al. The influence of diabetes, glycemic control, and diabetes-related comorbidities on pulmonary tuberculosis. PLoS One. 2015;10(3):e0121698.
19. Alisjahbana B, Sahiratmadja E, Nelwan EJ, Purwa AM, Ahmad Y, Ottenhoff THM, et al. The effect of type 2 diabetes mellitus on the presentation and treatment response of pulmonary tuberculosis. Clin Infect Dis. 2007;45(4):428–35.
20. Singla R, Khan N, Al-Sharif A, Al-Sayegh MO, Shaikh MA, Osman MM. Influence of diabetes on manifestations and treatment outcome of pulmonary TB patients. Int J Tuberc Lung Dis. 2006;10(1):74–9
21. Duangrithi D, Thanachartwet V, Desakorn V, Jitruckthai P, Phojanamongkolkij K, Rienthong S, et al. Impact of diabetes mellitus on clinical parameters and treatment outcomes of newly diagnosed pulmonary tuberculosis patients in Thailand. Int J ClinPract. 2013;67(11):1199–209.
22. Yurteri G, Sarac S, Dalkiliç O, Ofluoglu H, Demiröz F. Features of pulmonary tuberculosis in patients with diabetes mellitus: a comparative study. Turkish Respiratory J. 2004;5(1):5–8.
23. Baghaei P, Tabarsi P, Abrishami Z, Mirsaeidi M, Faghani YA, Mansouri SD, et al. Comparison of pulmonary TB patients with and without diabetes mellitus type II. Tanaffos. 2010;9(2):13–20.
24. Faurholt-Jepsen D, Range N, PrayGod G, Jeremiah K, Faurholt-Jepsen M, Aabye MG, et al. The role of diabetes on the clinical manifestations of pulmonary tuberculosis. Trop Med Int Health. 2012;17(7):877–83.