ISSN 2515-8260 Volume 09, Issue 07, 2022

Original Research Article

To study the efficacy of DOTS therapy in newly diagnosed patients with pulmonary tuberculosis with and without associated diabetes mellitus

[1]Sharad S, [2]Bhardwaj G

Dr Sharad Saxena[1]Assistant Professor, Department of General Medicine, Government Medical College, Kota, Rajasthan, India
Dr GauravBhardwaj[2]Assistant Professor, Department of Chest and Tuberculosis, Rajasthan University of Health Sciences College of Medical Sciences (RUHS-CMS), Jaipur, Rajasthan, India

Corresponding Author:
Dr. Gaurav Bhardwaj (drbhardwajg@gmail.com)

Abstract

Background: There is an increase in incidence of tuberculosis (TB) despite successful implementation of directly observed treatment, short course (DOTS) in India. The burden of diabetes and tuberculosis is more in developing countries and these diseases often coexist. Suboptimal control of diabetes predisposes the patient to tuberculosis and is one of the common causes of poor response to anti-tubercular treatment.

Objective: To study the efficacy of DOTS therapy in newly diagnosed patients of pulmonary tuberculosis with and without associated diabetes.

Methods: The prospective study was conducted at the department of General Medicine, in Mahatma Gandhi Medical College and Hospital Jaipur a tertiary health care centre in Rajasthan. In the study patients were grouped into one having PTB with DM and other group PTB without DM. Informed written consent was obtained from all patients and their clinical features were recorded. DOTS treatment was initiated and patient were followed up monthly for sputum conversion and weight gain.

Results: A total of 60 patients (20 to >60 years) were enrolled in the study with equal numbers being grouped in the 2 categories i.e. PTB with DM and PTB-non DM. More sputum positivity 21(70%) was associated with diabetic group. Sputum conversion were seen in 3 patients in diabetic group whereas it is seen in 1 patient in non-diabetic group in 2-3 months. Average weight gain is more in non-diabetic as compared to diabetic patients.

Conclusions: Good glycaemic control is needed for effectiveness of DOTS therapy. Early screening and diagnosis of Diabetes in patients of pulmonary tuberculosis will definitely help in management of both the disease.

Keywords: Pulmonary tuberculosis, diabetes mellitus

Introduction

Tuberculosis (TB) remains a major source of morbidity and mortality throughout the world with one-third of the world's population infected with Mycobacterium tuberculosis. Approximately nine million people develop disease every year and almost two million die annually from the disease [1, 2]. Epidemiological studies have shown an association between diabetes mellitus (DM) and the development of TB [3-7]. Also people with DM had approximately three times the risk of developing TB disease as people without [4].

The global burden of DM is rising; the prevalence is estimated to reach 438 million by 2030 with more than 80% of the adult cases increasing in newly developed or developing countries [8]. This will lead to an increased incidence of TB, especially in low and middle income countries with increasing numbers of people with DM and prevalent TB disease [5, 9].

TB infection also deteriorates the glycemic control and reduces the effectiveness of DM

ISSN 2515-8260 Volume 09, Issue 07, 2022

management [10].The patients of pulmonary TB with DM experienced poor rate of sputum conversion at the end of 2-month regimen along with higher rates of treatment failure as compared to non-DM patients [11-13].

The treatment of pulmonary tuberculosis with DM is a challenge in the present day scenario due to its increasing coexistence. Also uncontrolled DM is responsible for poor clinical response to anti-tuberculosis treatment. The present study was undertaken to evaluate the clinically efficacy of DOTS therapy in diabetic and non-diabetic patients.

Materials and Methods

The present study was done in Department of General Medicine, MGUMST, Jaipur [RAJ] from July 2015 to July 2016.

The Institutional Ethics Committee permission was taken for the study. A prospective study including 60 patients of pulmonary tuberculosis was diagnosed by detailed history, clinical examination, sputum examination for acid fast bacilli, chest radiography. Diabetes mellitus was diagnosed as per ADA criteria. Patients were grouped as pulmonary tuberculosis with Diabetes Mellitus and pulmonary tuberculosis without Diabetes Mellitus. Adult patients who fulfilled the criteria were included in the study. After taking consent, patients were examined in detail and subjected to relevant laboratory and radiological investigations. A proforma was filled by interviewing the patients and clinical examination was done.

Inclusion Criteria

- Age >18 yrs.
- Diabetic on insulin or OHA or both.
- Clinical features and or radiology consistent with pulmonary tuberculosis and or positive sputum for AFB.

Exclusion criteria

- Cases (defaulter, relapse, failure).
- Pulmonary tuberculosis patients with age <18 years.
- Patients with HIV.
- Patients on steroids or any other form of immunosuppressive therapy.
- Patients not willing for regular follow up.
- All extrapulmonary tuberculosis patients.
- History of known close contacts of drug-resistant pulmonary tuberculosis and already diagnosed drug-resistant pulmonary tuberculosis patients.

Efficacy of treatment was gauged by

Pulmonary tuberculosis

1. **Clinical improvement:** Defined by improvement in cough, fever, weight gain and sense of well-being, review according to RNTCP guidelines upto completion of therapy.

2. **Sputum conversion:** Examination of sputum smear for AFB as per RNTCP guidelines.

Diabetes mellitus

a. Plasma glucose monitoring- both fasting and P.P. checked monthly.
b. HbA1c once in 3 months.

Statistical method

- For different qualitative parameters mean and standard deviation calculated.
- To compare the means between two groups, student unpaired ‘t’ test is used.

ISSN 2515-8260 Volume 09, Issue 07, 2022

Level of significance is taken as $p<0.05$.

- Chi square test is used to find the association between two qualitative variables.

Statistical analysis

The data was coded and entered into Microsoft Excel spreadsheet. Analysis was done using SPSS version 20 (IBM SPSS Statistics Inc., Chicago, Illinois, USA) Windows software program. The variables were assessed for normality using the Kolmogorov Smirnov test. Descriptive statistics included computation of means and standard deviations. Level of significance was set at $p\leq 0.05$.

Observations and Results

In our study in pulmonary tuberculosis, of which 30 were diagnosed cases of diabetes mellitus(DM) and 30 of non DM group. All were registered in DOTS and followed up monthly for sputum conversion and weight gain.

Table 1: Distribution of cases according to Treatment of diabetes

S. No.	Treatment Given	II DM	%
1.	OHA	22	73.33
2.	Insulin	-	-
3.	Both	8	26.67
Total		30	

Table 2: Distribution of cases according to Initial Investigation

S. No.	Investigation	Pulmonary Tuberculosis				Total
		Diabetes Mellitus		Non diabetic		
		No.	%	No.	%	
1.	Hb (low)	17	56	18	60.0	35
2.	ESR (raised)	27	90	30	100	57
3.	Urea (raised)	3	10	-	-	3
4.	Creatinine (raised)	3	10	-	-	3

Table 3: Distribution of cases according to sputum positivity

S. No.	Sputum	Pulmonary Tuberculosis				Total
		Diabetes Mellitus		Non diabetic		
		No.	%	No.	%	
1.	Negative	9	30	12	40	21
2.	Positive	21	70	18	60	39
Total		30		30		60

Table 4: Distribution of cases according to extent of tuberculosis and duration of diabetes

S. No.	Extent of TB (Radiological)	Duration of diabetes		
		<5 yrs	5-10 yrs	>10 yrs
1.	Minimal	1	3	2
2.	Moderately advanced	2	4	5
3.	Far Advanced	4	2	7
Total		7	9	14

ISSN 2515-8260 Volume 09, Issue 07, 2022

Table 5: Distribution of cases according to duration for sputum conversion

S. No.	Sputum Conversion	Pulmonary Tuberculosis				
		Diabetes Mellitus			Non diabetic	
		2 Months	3 Months	5 Month	2 Months	3 Months
	Positive	6	11	1	14	3
	Negative	3			1	

Table 6: Distribution of cases according to average weight gain

S. No.	Category of Patient	Avg. wt gain in 6 months
1.	Non Diabetic	5.2
2.	Diabetic	4.6

Table 7: Distribution of cases according to side effects

S. No.	Side effects	Pulmonary Tuberculosis				Total
		Diabetes Mellitus		Non diabetic		
		Total	%	No.	%	
1.	Nausea	8	26.66	6	20.00	14
2.	Vomiting	5	16.66	6	20.00	11
3.	Epigastric pain	7	23.33	9	30.00	16
4	Deranged LFT	19	63.33	17	56.67	36
5	Peripheral neuropathy	3	10.00	1	3.33	4

A total of 22 patients (73.33) were on oral hypoglycemic agents (OHA) and 8(26.67%) were on combined OHA and insulin therapy. None of the patients were on single insulin therapy alone.

Haemoglobin (Hb) was low more in non- diabetic 18(60%) as compared to diabetic 17(56%) patients; while ESR was comparably raised in both diabetic 27(90%) and non-diabetic group 30 (100%). Deranged renal function test were seen in diabetic group 3(10%).

Out of 30 patients in diabetic group 21 (70%) are sputum positive and 9 (30%) are sputum negative. Whereas out of 30 patients in non-diabetic group 18 (60%) are sputum positive and 12 (40%) are sputum negative.

Majority of patients with far advanced lesion 7 had duration of diabetes >10 yrs. This suggests that as duration of diabetes increases, severity of lesion increases.

In our present study X-ray at presentation was minimal 20%, moderately advanced 36.66% and far advanced 43.33%.

Sputum Conversion was negative in three patients in second and third month and out of these two were lost to follow up in fourth month in diabetic group.

Sputum Conversion was negative in one patient in second and third month and it was lost to follow up in fourth month in non-diabetic group.

In our present study average weight gain is 5.2 in non-diabetic group as compared to diabetic group i.e. 4.6. Average weight gain is more in non-diabetic as compared to diabetic.

In the present study in diabetic group most side effects seen were nausea (26.66%), vomiting (16.66%), epigastric pain (23.33%), deranged liver function test (63.33%) and peripheral neuropathy (10%).

In non-diabetic group most side effects seen were nausea (20.00%), vomiting (20.00%), epigastric pain (30.00%), deranged liver function test (56.67%) and peripheral neuropathy (3.33%).

Discussion

The present study consisted of 60 diagnosed patients of pulmonary tuberculosis. Thirty of these were diagnosed cases of diabetes coming to OPD and ward. Both groups were registered in DOTS and followed up monthly.

ISSN 2515-8260 Volume 09, Issue 07, 2022

In our present study out of 30 diabetic patients 73.33% were on OHA whereas 26.66% were on both [insulin and OHA].

Hemoglobin was low in 56% in diabetic group and 60% in non-diabetic group. ESR was increased in 90% in diabetic group and 100% in non-diabetic group and urea and creatinine was increased in 10% in diabetic group only.

Lee *et al*. [14] supported the prevalence of low haemoglobin in TB patients and Khalil NH [15] also observed low Hb in TB-DM patients.

Alisjhabana B *et al*. [16], Bashir *et al*. [17] also observed high ESR in their respective studies.

In our present study out of 30 patients in diabetic group 21 (70%) are sputum positive and 9 (30%) are sputum negative. Whereas out of 30 patients in non-diabetic group 18 (60%) are sputum positive and 12 (40%) are sputum negative.

The observations of the study are consistent with those of by Shital P *et al*. [18], R. Singla *et al*. [19], Fengling MI *et al*. [20].

Majority of patients with far advanced lesion 7 had duration of diabetes >10 yrs. This suggests that as duration of diabetes increases, severity of lesion increases.

In our present study X-ray at presentation was minimal 20%, moderately advanced 36.66% and far advanced 43.33%.

In the study done by Vellalacheruvu BN [21] *et al*. study X ray at presentation was minimal 12.5%, moderately advanced 31.2% and far advanced 56.2%. Our data is similar to study done by by Vellalacheruvu BN *et al*. [21].

In the present study 21 patients were sputum positive in diabetic group out of which sputum conversion was positive in 6 patients (28.57%) in 2 month, 11 patients (57.14%) in 3 month, 1 patient (4.76%) in 5 month. Sputum conversion was negative in 3 patients in second and third month and out of these two were lost to follow up in fourth month. 18 patients were sputum positive in non-diabetic group out of which sputum conversion was positive in 14 patients (77.77%) in 2 month, 3 patients (16.6%) in 3 month. Sputum conversion was negative in 1 patient in second and third month and it was lost to follow up in fourth month.

In the study done by R. Singla *et al*. [19] sputum conversion rates were analysed. At the end of the 2-month intensive phase of treatment, 83.8% of the patients in the PTB-DM group had achieved sputum conversion compared to 90.7% in the PTB group. At the end of 3 months of treatment, 98.9% of patients in the PTB-DM group achieved sputum AFB smear conversion compared to 94.7% in the PTB group [19].

In the study done by Vellalacheruvu BN [21] *et al*. sputum conversion rates were analysed. At the end of 2 months Negative in 62.5% (20) of patients with DM and 79.7% (51) of patients without DM. Positive in 12.5% (4) of patients with DM and 9.4% (6) of patients without DM. Sputum conversion was more in non-diabetic group as compared to diabetic group.

In the study done by Alisjahbana B [16] *et al*. showed sputum conversion rates of 71.3% in patients with DM and 84.3% in patients without DM.

In the study done by Siddiqui AN[22] *et al*. Microscopic examination of sputum samples at 2 months reveals higher sputum positivity in DM (27.8%) as compared to no-DM (24.7%) patients. Logistic regression analysis showed that DM with TB patients had a higher probability of delayed sputum conversion and poor treatment outcome) as compared to no-DM patients.

In the study done by Shital P *et al*. [18] sputum conversion percentage was found significantly lesser in study cases with diabetic group as compared to non-diabetic group i.e. 76.53% versus 92.70% respectively.

In the study done by by Jumaev G *et al*. [23] sputum conversion rates were analysed. Sputum conversion in diabetic group was 75% in 2 month and 12% in 3 month whereas in non-diabetic group it was 84% in 2 month and 9% in 3 month.

In our present study average weight gain is 5.2 in non-diabetic group as compared to diabetic group i.e. 4.6. Average weight gain is more in non-diabetic as compared to diabetic.

In the study done by Faurholt-Jepsen D *et al*. [24] within the initial two months of treatment, TB patients with diabetes co-morbidity experienced a 1.3 kg lower weight gain compared to

ISSN 2515-8260 Volume 09, Issue 07, 2022

the non-diabetic group. The delayed weight gain sustained at five months of TB treatment, with a 1.0 kg lower weight gain among TB patients with diabetes co-morbidity.
In the study done by Vasantha M *et al*. [25] an average of 3.34 kg weight gain was seen in tubercular patients.
In the present study in diabetic group most side effects seen were nausea (26.66%), vomiting (16.66%), epigastric pain (23.33%), deranged liver function test (63.33%) and peripheral neuropathy (10%).
In non-diabetic group most side effects seen were nausea (20.00%), vomiting (20.00%), epigastric pain (30.00%), deranged liver function test (56.67%) and peripheral neuropathy (3.33%).
In the study done by Siddiqui AN [22] *et al*. side effects seen in diabetic group was nausea and vomiting (26.8%), liver injury (17.1%) and peripheral neuropathy (34.1%) whereas in non-diabetic group nausea and vomiting (17.7%), liver injury (15%) and peripheral neuropathy (21%). In this study side effects were more seen in diabetic group.

Conclusion

Diabetic patients have an increased risk of TB. Both the diseases affect each other. DM predisposes a person to TB, which in turn disrupt metabolic control. Effective control of each affects the control of the other condition. Active screening measures for DM are recommended in patients with TB which can improve the diagnosis and help in early management of DM and its complications. There is a need of studying the effect of long-term evolution of DM control and associated complications on TB treatment outcome. Glycemic control should be strictly maintained, particularly, during the initial intensive phase for better outcome in patients with DM.

References

1. Lonnroth K, Raviglione M. Global epidemiology of tuberculosis: prospects for control. Semin Respir Crit Care Med. 2008;29:481-491.
2. World Heath Organization: Global tuberculosis control 2009: epidemiology, strategy, financing. Geneva, Switzerland; c2010. [http://www. who.int/tb/publications/global_report/2009/en], WHO/HTM/TB/2009.411.
3. Ponce-De-Leon A, Garcia-Garcia Md. Mde L, Garcia-Sancho MC, Gomez Perez FJ, Valdespino-Gomez JL, Olaiz-Fernandez G, *et al*.: Tuberculosis and diabetes in southern Mexico. Diabetes Care. 2004;27:1584-1590.
4. Jeon CY, Murray MB. Diabetes mellitus increases the risk of active tuberculosis: a systematic review of 13 observational studies. PLoS Med. 2008;5:e152.
5. Stevenson CR, Forouhi NG, Roglic G, Williams BG, Lauer JA, Dye C, *et al*.: Diabetes and tuberculosis: the impact of the diabetes epidemic on tuberculosis incidence. BMC Public Health. 2007;7:234.
6. Kim SJ, Hong YP, Lew WJ, Yang SC, Lee EG. Incidence of pulmonary tuberculosis among diabetics. Tuber Lung Dis. 1995;76:529-533.
7. Dooley KE, Chaisson RE: Tuberculosis and diabetes mellitus: convergence of two epidemics. Lancet Infect Dis. 2009;9:737-746.
8. International Diabetes Federation: Diabetes Factsand Figures. Diabetes Prevalence; c2009. [http://www.idf.org/diabetes-prevalence].
9. Restrepo BI: Convergence of the tuberculosis and diabetes epidemics: renewal of old acquaintances. Clin. Infect Dis. 2007;45:436-438.
10. The Lancet Diabetes & Endocrinology, Diabetes and tuberculosis-a wake-up call, The Lancet Diabetes & Endocrinology. 2014;2(9):677.
11. Morsy AM, Zaher HH, Hassan MH, Shouman A. Predictors of treatment failure among tuberculosis patients under DOTS strategy in Egypt, Eastern Mediterranean Health Journal. 2003;9(4):689-701.
12. Dooley KE, Tang T, Golub JE, Dorman SE, Cronin W. Impact of diabetes mellitus on

treatment outcomes of patients with active tuberculosis, The American Journal of Tropical Medicine and Hygiene. 2009;80(4):634-639.

13. Wang CS, Yang CJ, Chen HC, *et al*., Impact of type 2 diabetes on manifestations and treatment outcome of pulmonary tuberculosis, Epidemiology and Infection. 2009;137(2):203-210.
14. Lee SW, Kang YA, *et al*. The prevalence and evolution of anemia associated with tuberculosis J Korean Med. Sci. 2006;21(6):1028-1032.
15. Khalil NH, Ramadan RA. Study of risk factor for pulmonary tuberculosis among diabetes patients. Egyptian journal of Chest diseases and Tuberculosis. 2016 Oct ;65(4):817-823.
16. Alisjahbana B, Sahiratmadja E, *et al*. The effect of type 2 diabetes mellitus on the presentation and treatment response of pulmonary tuberculosis Clin. Infect. Dis. 2007;45:428-435.
17. Bashir AB, Ageep Ali K, *et al*. Reactive Thrombocytosis and Erythrocyte Sedimentation Rate in Patients with Pulmonary Tuberculosis Sudan, Medical laboratory science, 2014.
18. 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 Pulm. Respir. Med. 2014;4(175):2.
19. Singla R, Khan N, Al-Sharif N, Al-Sayegh MO, Shaikh MA, Osman MM. Influence of diabetes on manifestations and treatment outcome of pulmonary TB patients. The International Journal of Tuberculosis and Lung Disease. 2006 Jan;10(1):74-9.
20. Mi F, Tan S, Liang L, Harries AD, Hinderaker SG, Lin Y, *et al*. Diabetes mellitus and tuberculosis: pattern of tuberculosis, two-month smear conversion and treatment outcomes in Guangzhou, China. Tropical Medicine & International Health. 2013 Nov;18(11):1379-85.
21. Vellalacheruvu BN, Bekur R, Mapakshi H. Effect of type 2 Diabetes mellitus on Presentation and Treatment response of Sputum positive Pulmonary Tuberculosis. International Journal of Scientific and Research Publications, 2015 Sept;5(9):2250-3153.
22. Siddiqui AN, Khayyam KU, Sharma M. Effect of diabetes mellitus on tuberculosis treatment outcome and adverse reactions in patients receiving directly observed treatment strategy in India: a prospective study. Bio Med Research International, 2016 Aug.
23. Jumaev G, Tillashaykhov M, Muazzamov B, Radjabov B, Gadoev J, Alikhanova N, *et al*. Prevalence, characteristics and treatment outcomes of all patients with new tuberculosis and diabetes mellitus in 2011-2013, Bukhara, Uzbekistan. Public health panorama. 2016 March;2(1):1-116.
24. Faurholt-Jepsen D, Range N, Praygod G, Kidola J, Faurholt-Jepsen M, Aabye MG, *et al*. The role of diabetes co-morbidity for tuberculosis treatment outcomes: a prospective cohort study from Mwanza, Tanzania. BMC infectious diseases. 2012 Jul;12(1):165.
25. Vasantha M, Gopi PG, Subramani R. Weight gain in patients with tuberculosis treated under directly observed treatment short-course (DOTS). Indian J Tuberc. 2009 Jan;56(1):5-9.