RESEARCH PAPER | Medical Science | Volume : 6 | Issue : 3 | March 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

Prevalence and Drug Resistance Pattern Among Diabetic Pulmonary Tuberculosis Patients Treated Under RNTCP

KEYWORDS: Diabetes; Tuberculosis; Drug Resistance.

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ABSTRACT *INTRODUCTION: - Tuberculosis has been a major cause of suffering and death since time immemorial. Thought to be one of the oldest human diseases, the history of tuberculosis is at least as old as the mankind. People with diabetes have 2-3 times higher risk of TB compared to people without diabetes. About 10% of TB cases globally are linked to diabetes. Management of Tuberculosis becomes a bit difficult with diabetes as a comorbid condition as poor glycemic control. Hence therefore we have planned this study "Prevalence And Drug Resistance Pattern Among Diabetic Pulmonary Tuberculosis Patients Treated Under RNTCP".*

AIMS and OBJECTIVES:-

1. *Prevalence of Diabetes mellitus among Tuberculosis patients registered under RNTCP.*
2. *Drug sensitivity pattern among smear positive retreatment diabetic patients.*

MATERIALS AND METHODS: This study was conducted in The Department of Respiratory Medicine, JLN Medical College, Ajmer from 1st January 2012 to 31st December 2012.

RESULTS: - Most of the patients were between 31 to 60 years (75.01%) and maximum (39.30%) in 41 to 50 years. There is an overall male predominance with male female ratio 2.1:1. The prevalence of diabetes mellitus among patients of tuberculosis was 7.356. Type-2 diabetes mellitus was present in 94.05% patients. In 75% patients were Rifampicin and Isoniazid resistant. In 75% patients Rifampicin and Isoniazid resistant were present in those in which HBA1c level was >8.0 and in 25% patients Rifampicin and Isoniazid sensitive in which HBA1c level was up to 7.0.

INTRODUCTION

Tuberculosis has been a major cause of suffering and death since time immemorial. Thought to be one of the oldest human diseases, the history of tuberculosis is at least as old as the mankind[1]. In 1993 WHO declared Tuberculosis is a global emergency, saying the disease will claim more than 30 million lives in the next decade unless action is taken now. Manager WHO Tuberculosis program, Arati Kochi, state that Tuberculosis today is greater killer, and it is out of control in many parts of world. The disease preventable and treatable has been grossly neglected and no country immune to it[2,3]. According to WHO Global TB Report 2012 Indian led the largest number of tuberculosis cases (about 2-2.5 million)[3].People with a weak immune system, as a result of chronic diseases such as diabetes, are at an increased risk of progressing from latent to active TB. People with diabetes have 2-3 times higher risk of TB compared to people without diabetes. About 10% of TB cases globally are linked to diabetes[4]. In sep. 2011, WHO estimated that 350 million people were living with diabetes. Diabetes prevalence is similar in both high and low income countries and over 80% of deaths occur in low and middle income countries. It is predicted that global diabetes prevalence will increase by 50% by 2030[5] and 80% of prevalent cases will occur in the developing world[5]. This dual epidemic is going to affect us significantly in very near future due to emergence of multidrug resistance, extreme drug resistance and Total drug resistance tuberculosis. Lately World Health Organisation also recognised this potential time bomb and accordingly has published a vision document to undertake future research in this direction to have sufficient data base to formulate effective strategies to check this seemingly contains booming large catastrophic on mankind[3]. There is insufficient data in Rajasthan on this subject hence therefore we have planned this study "Prevalence And Drug Resistance Pattern Among Diabetic Pulmonary Tuberculosis Patients Treated Under RNTCP".

AIMS AND OBJECTIVE

1. Prevalence of Diabetes mellitus among Tuberculosis patients registered under RNTCP.
2. Drug sensitivity pattern among smear positive retreatment diabetic patients.

MATERIAL AND METHODS

This study was conducted in The Department of Respiratory Medicine, JLN Medical College, Ajmer from 1st January 2012 to 31st December 2012.

All Diabetic Patients registered under all categories of RNTCP - Category-I, Category-II and DOTS plus (Category IV) were included in this study who were admitted in the department.

Diagnosis of Tuberculosis was based upon demonstration

Volume : 6 | Issue : 3 | March 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

of Acid Fast Bacilli in sputum microscopy, Mycobacterial culture, Fine Needle Aspiration Cytology, Bronchoscopic brushings or lavage. Patients with radiologic features suggestive of tuberculosis in case of abdominal tuberculosis or Bone tuberculosis (USG, CT, or X-ray of Bone, Barium study) have been considered as a case of tuberculosis.

Fasting and 2 hour post-parandial blood glucose have been measured in all patients. In known diabetic patients, an additional HbA1c were measured. Glucose tolerance test would do to diagnose latent diabetics and pre diabetics.

All these patients have been followed up at the time of RNTCP protocol with fasting blood sugar, HbA_1c. Sputum examination and Radiographic examinations were done as per RNTCP protocols.

The clinical and radiological assessment were regularly assessed and recorded till the completion of intensive phase.

Mycobacterial Culture and Sensitivity done by Line Probe Assay and on Lowenstein Jenson media at State Tuberculosis and Demonstration Centre (IRL) Ajmer.

Statistical assessment done by "PRIMER STATISTICAL SOFTWARE VERSION-6".

RESULTS

Table 1 shows Age and Sex distribution in case and control group. From above table it is clear that majority of cases (n=63, 75.01%) were between 31 to 60 years of age, the maximum number 33(39.30%) being in the age 41 to 50 years in study population. In case group male 57 (67.90%) seen more frequently in as compared to female 27 (32.10%) and in control group male 60 (74.07%) were more than female 21 (25.93%) which were almost same in both group. Mean age in case group is 49.33 years and in control group 40 years. Male to Female ratio was 2.1:1in case group and in control group 2.85:1.

79 (94.05%) cases were type 2 Diabetes Mellitus and only 5 (5.95%) cases were type 1 Diabetes Mellitus. (Table 2)

84 Diabetic patients, 23 (27.38%) patients are newly diagnosed cases of Diabetes Mellitus and remaining 61 (72.62%) patients were previously known cases of Diabetes Mellitus who had tuberculosis.(Table 3). almost similar proportion of pulmonary and extra pulmonary tuberculosis in case and control group. P value by Fisher's exact test is >0.05 which is statistically not significant. (Table 4)

In type 1 Diabetes Mellitus 3 (75%) cases were smear positive and 1(25%) case was smear negative and in type 2 Diabetes Mellitus 46 (65.71%) cases were smear positive and 24 (34.29%) were smear negative. Smear status at the time of diagnosis was not statistically significant (P value, >0.05). (Table 5).uniform distribution of smear positive cases with HBA1c level 7 or above suggesting that level of glycemic control did not affect smear status in case group at the time of presentation.(Table 6)

Out of case group, at the end of intensive phase 1(25%) patient was rifampicin and isoniazid sensitive and 3(75%) patients were rifampicin and isoniazid resistant. Only one patient who was found to be sputum positive at the end of intensive phase in control group was also resistant to rifampicin and isoniazid. The difference between both the groups was not statistically significant (p value, >0.05). (Table 7)

Only 1 (25%) patient was Rifampicin & Isoniazid sensitive which had HBA1c level in range up to 7.0. Rifampicin & Isoniazid resistant were 3 patients, 1 (25%) in each 8.1 to 9.0, 9.1 to 10.0 and >10.0 HBA1c levels. (Table 8).

DISCUSSION

The present case control study was carried out in the Department of Respiratory Medicine, JLN Medical College, Ajmer. 165 cases were treated both in case group (DM-TB) and control group (TB without DM). Their demographic profile, sputum smears at time of diagnosis and follow-up along with skiagram chest, other relative haematological and biochemistry investigations along with HB1c.

About 10% of TB cases globally are linked to diabetes. People with diabetes have a 2-3 times increased risks of TB compare to people without Diabetes. Weak immune systems, as a result of chronic diseases such as diabetes, are at a higher risk of progressing from latent to active TB. A large proportion of people with diabetes as well as TB is not diagnosed, or is diagnosed too late. Early detection can help improve care and control of both[4].The most recent estimates of the global burden of diabetes mellitus (DM) come from the 2011 Diabetes Atlas of the International Diabetes Federation. Diabetes has been shown to be an independent risk factor for tuberculosis in community based study from South India and multiple studies globally[6]. Mona Bashar et al (1987-1997), in their study of 50 cases suggested that Diabetic are more susceptible to have a more aggressive course of tuberculosis diseases possibly due to impaired GI drug absorption even in the absence of clinical gastroparesis. Most of the patients were between 31 to 60 years (75.01%) and maximum (39.30%) in 41 to 50 years. There is an overall male predominance with male female ratio 2.1:1. The prevalence of diabetes mellitus among patients of tuberculosis was 7.356. Type-2 diabetes mellitus was present in 94.05% patients.

Deshmukh P. A. et al (1984) suggested that prevalence of diabetes was 5.6% (n138) in 2434 cases of pulmonary tuberculosis and it increase with age[7]. Ponce de leon et al suggested in his study from march 1995 to march 2003 at Mexico suggested that in 581 patients with mycobacterium tuberculosis were diagnosed with culture and fingerprint, in which 29.6%dignosed previously were with Diabetes, the estimated prevalence of diabetes in the study area was 5.3% and the rate of tuberculosis was increase 6.8 fold (95% CI 5.7-8.2, P<o.ooo1)[8]. In the present study 88.10% of the patients were having pulmonary tuberculosis (new=52.38%, relapse=14.29%, multidrug-resistant=21.43%) and rest 11.90% cases were extra-pulmonary tuberculosis (pleural effusion=8.33%, Lymphadenopathy=1.19, Pyopneumothorax=1.19%, pericardial effusion=1.19%). A study by Catherine R Stevenson et al (2007) showed that in India 18.4%(12.5% to 29.9%) of people with pulmonary TB (both smear positive and smear negative) have diabetes, and that in smear positive group diabetes prevalence is 23.5%(12.1% to 44%)[9]. Mullen and Higgins (1961) observed 4.2% prevalence of diabetes in 118 tuberculosis patients in a tuberculosis sanatorium in Alberta, Canada[10]. Blum and Atagun (1963) reported 3.84% prevalence of diabetes in 2342 tuberculosis patients from January 1953 to December 1960 at Baltimore city hospital[10]. According to WHO about 10% of TB cases globally are linked to diabetes[4]. According to TB India 2012 diabetes accounts for 14.8% of all tuberculosis and

Volume : 6 | Issue : 3 | March 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

20.8% of smear-positive TB[6]. Maria Eugenia Jimenez Corona et al (2012) observed in his study of patients with tuberculosis in Southern Maxico from 1995 to 2010 showed the prevalence of DM among 1262 patients with pulmonary TB was 29.63% (n=374)[11].

Nissapatorn V et al observed in his study from January 2001 to December 2002 showed that TB-DM patients had a higher ratio of male to female (69.3% v/s 30.7% respectively) than TB group(65% v/s 35% respectively). Qazi M. A. et al reported in this study at B. V. Hospital Bahawalpur from January 2004 to December 2006 in 150 pt's with DM [both type 1(11.33% pt's) and type 2(88.67% pt's)] and PTB. In this study 105 were male (70%) and 45 females (30%) and mean age 49.81 (18 to 75) years. In 75% patients were Rifampicin and Isoniazid resistant. In 75% patients Rifampicin and Isoniazid resistant were present in those in which HBA1c level was >8.0 and in 25% patients Rifampicin and Isoniazid sensitive in which HBA1c level was up to 7.0. Globally, 3.7% (2.1-5.2%) of new cases & 20% (13-26%) of previously treated cases are estimated to have MDR-TB. There were estimated 310000 (range 220000-400000) MDR-TB cases among notified TB pt's with PTB in 2011. Almost 60% of these cases were on India, china and Russian Federation. Globally, almost 60000 cases of MDR-TB were notified to WHO in 2011 which were just 19% of estimated cases. Globally, <4% of new bacteriological positive cases and 6% of previously treated cases were tested for MDR-TB in 2011. The ratio of notified MDR-TB cases to number of pt's starting treatment with II line drug regimen for MDR-TB was almost 1.1% globally[3].Carreira S et al reported in his study from 2000 to 2008 in which TB with DM showed MDR-TB in 4.1% patients and TB without DM group showed 4.9%.Singla R et al (2006) observed in this study at Sahary Chest Hospital, Riyadh, Saudi Arabia on 187 DM-PTB (27%) and 505 PTB (73%) pt's. Drug sensitivity test (DST) was available for 126 DM-PTB and 389 PTB pt's. significantly fewer PTB-DM pt's had resistance to any one of the anti-tuberculosis drugs compare to PTB group (6.3% v/s 18.3%, respectively p=0.001 in all cases and for new cases 6.4% v/s 16%, respectively p=0.007).

Conclusion:

Diabetes and tuberculosis are complementary to each other. Present study has shown diabetic people with tuberculosis are more prone to develop MDR tuberculosis. Association with HBA1c with drug resistance has also been proved, so it demands more multi centric studies with larger sample size to validate these findings.

TABLES

Table No. 1

Age & sex distribution among case group (DM-TB) and control group (TB)

Age in years	Case group n=84			Control group n=81		
	Male n (%)	Female n (%)	Total	Male n (%)	Female n (%)	Total
Upto 20	1 (1.19%)	1 (1.19%)	2 (2.38%)	3 (3.70%)	6 (7.41%)	9 (11.11%)
21-30	3 (3.57%)	1 (1.19%)	4 (4.76%)	10 (12.35%)	6 (7.41%)	16 (19.76%)
31-40	11 (13.10%)	3 (3.57%)	14 (16.67%)	13 (16.05%)	6 (7.41%)	19 (23.46%)
41-50	22 (26.20%)	11 (13.10%)	33 (39.30%)	20 (24.70%)	2 (2.46%)	22 (27.16%)
51-60	7 (8.33%)	9 (10.71%)	16 (19.04%)	6 (7.41%)	1 (1.23%)	7 (8.64%)
61-70	9 (10.71%)	1 (1.19%)	10 (11.90%)	7 (8.64%)	0	7 (8.64%)
>70	4 (4.76%)	1 (1.19%)	5 (5.95%)	1 (1.23%)	0	1 (1.23%)
Total	57(67.90%)	27 (32.10%)	84(100%)	60 (74.07%)	21 (25.93%)	81(100%)

Table No. 2

Distribution of types of Diabetes Mellitus among case group (DM-TB)

Type of Diabetes Mellitus	Total no. of cases, n=81	%
Type 1 Diabetes Mellitus	5	5.95 %
Type 2 Diabetes Mellitus	79	94.05 %
Total	84	100

Table No. 3

Newly diagnosed versus known case of Diabetes mellitus

Type of diagnosis Diabetes Mellitus	N	%
Newly diagnosed Diabetes Mellitus	23	27.38%
Known case of Diabetes Mellitus	61	72.62%
Total	84	100 %

Table No. 4

Type of tuberculosis among case group (DM-TB) and control group (TB)

Type of tuberculosis		Case group n =84	Control group n =81	P value
Pulmonary tuberculosis	Newly diagnosed	44 (52.38%)	44 (54.32%)	>0.05
	Relapse	12 (14.29%)	12 (14.81%)	
	Multidrug-resistant	18 (21.43%)	15 (18.52%)	
	Total	74 (88.10%)	71 (87.65%)	
Extra pulmonary tuberculosis		10 (11.90%)	10 (12.35%)	
Total		84	81	

Table No. 5

Type of Diabetes Mellitus and smear status at the time of diagnosis in pulmonary tuberculosis

Smear status at time of diagnosis	Type 1 Diabetes Mellitus	Type 2 Diabetes Mellitus	Total	P value
Smear positive (n=46)	3 (75%)	46 (65.71%)	49 (66.22%)	>0.05
Smear negative (n=25)	1 (25%)	24 (34.29%)	25 (33.78%)	
Total	4	70	74	

Volume : 6 | Issue : 3 | March 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

Table No. 6
HBA1c and smear positivity in different type of case group (DM-TB), n=34

HBA1c level	New cases	Relapse cases	Multidrug-resistant cases	Total
Up to 7.0	3 (8.83%)	0	0	3 (8.83%)
7.1 to 8.0	5 (14.71%)	4 (11.76%)	0	9 (26.47%)
8.1 to 9.0	4 (11.76%)	2 (5.88%)	1 (2.94%)	7 (20.58%)
9.1 to 10.0	5 (14.71%)	1 (2.94%)	1 (2.94%)	7 (20.59%)
>10.0	5 (14.71%)	2 (5.88%)	1 (2.94%)	8 (23.53%)
Total *	22 (64.71%)	9 (26.46%)	3 (8.82%)	34

*= in remaining 15 MDR patients we could not do HBA1c level

Table No. 7
Pattern of drug resistance if sputum positive at end of intensive phase in case group (DM-PTB) and control group (PTB)

Sensitivity pattern	Case group n=4	Control group n=1	P value
Rifampicin & isoniazid sensitive	1(25%)	0	>0.05
Rifampicin & isoniazid resistant	3(75%)	1(100%)	

Table No. 8
HBA1c and drug resistance among study group (DM-TB), n=4

HBA1c level	Rifampicin & Isoniazid sensitive	Rifampicin & Isoniazid resistant
Upto 7.0	1 (25%)	0
7.1 to 8.0	0	0
8.1 to 9.0	0	1 (25%)
9.1 to 10.0	0	1 (25%)
>10.0	0	1 (25%)

References:

1. Surendra K. Sharma. Text book of Tuberculosis. Second edition 2009. Chapter No. 2: History- Alladi Mohan, SK Sharma.
2. World Health Organisation. Tuberculosis. Fact Sheet No 104 Revised August 2002.
3. WHO Global TB Report 2012.
4. WHO Sep 2011Tuberculosis & Diabetes,www.who.int/tb.
5. Collaborative Framework For care and control of tuberculosis and diabetes;WHO/HTM/TB/2011.15
6. TB INDIA 2012
7. Deshmukh PA and Shaw T. Pulmonary tuberculosis and diabetes mellitus. Ind J Tuberc 1984; 31: 114-17.
8. Ponce-De-Leon A, Garcia-Garcia Md Mde L, Garcia-sancho13. Ponce-De-Leon A, Garcia-Garcia Md Mde L, Garcia-sancho MC, Gomez-Perez FJ, Valdespino-Gomez JL, et al. Tuberculosis and diabetes in southern Mexico. Diabetes Care 2004; 27:1584-90.
9. 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. Joslin's Diabetes Mellitus; 11th edition: Philadelphia, 1971. María Eugenia Jiménez-Corona, Luis Pablo Cruz-Hervert, Lourdes García-García, Leticia Ferreyra-Reyes, Guadalupe Delgado-Sánchez, Miriam Bobadilla-del-Valle et al. Association of diabetes and tuberculosis: impact on treatment and post-treatment outcomes (http://dx.doi.org/10.1136/ thoraxjnl-2012-201756).