EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 5
Issue: 10
447-461
Year: 2018

CLINICAL PROFILE OF DIABETES MELLITUS IN ASSOCIATED PULMONARY TUBERCULOSIS

Dr. Ulhas Jadhav[1]*

Associate Professor in Department of Respiratory Medicine, AVBRH, Sawangi (Meghe), Wardha.

***Corresponding Author: Dr. Ulhas Jadhav**
Associate Professor in Department of Respiratory Medicine, AVBRH, Sawangi (Meghe), Wardha.

Article Received on 22/08/2018 **Article Revised on 12/09/2018** **Article Accepted on 02/10/2018**

INTRODUCTION

Tuberculosis is a chronic bacterial infection caused by Mycobacterium tuberculosis and charecterized by the formation of granulomas in infected tissues and by florid cell-mediated hypersensitivity. The usual site of the disease is the lungs, but other organs may be involved. In the absence of effective treatment, a chronic wasting course is usual and death ultimately supervenes in most cases (31).

Diabetes Mellitus is a heterogenous primary disorder of carbohydrate metabolism with multiple etiologic factors that generally involve absolute or relative insulin deficiency or insulin resistance or both. All causes of diabetes ultimately lead to hyperglycemia, which is the hallmark of this disease syndrome (16).

Diabetes Mellitus and Pulmonary Tuberculosis are major killers of mankind both being known since ages back. Initially both these diseases were studied by different workers seperately regarding their etio-pathogene- sis and management. During extensive studies it was found that these diseases frequently occur in association and pose very serious problems for the management.

This association was first noted by Avicenna[1] (980-1027) and is now the accepted fact of clinical medicine. Advances in scientific knowledge have revolutionised the management of both the maladies. Improved diagnostic armamentarium has led to better appreciation of the combination of two diseases than before; but the cause of the association has been little understood.

It was generally believed in the past that Tuberculosis was the complication of Diabetes and this association of Pulmonary Tuberculosis was thought to be one sided. Root and Dickson[66] stated that tuberculous patients do not develop Diabetes with any greater freqency than non-tuberculous. The converse relationship i.e that patients with Tuberculosis have a high prevalence of Diabetes was untill the 1950's less widely acceptable.

Nichols (1957)[53] in his study found evidence of glucose intolerance using an oral glucose tolerance test in 22 percent of 178 subjects with Tuberculosis and 5 percent had Diabetes. Since that time most of the studies have shown that the prevalence of Diabetes is indeed greater in patients with Tuberculosis. Deshmukh[21] et al, who in his masterly study (1966) found 14% of the tuberculous patients above on Tuberculosis is as harmful as the impact of Tuberculosis on Diabetes and believed that tuberculous patients develop Diabetes probably more often than diabetic patients developing Tuberculosis. Missing or overlooking the presence of Diabetes in Pulmonary Tuberculosis leads to disastrous culmination. With this in view the present study undertaken to determine the incidence of Diabetes Mellitus in Pulmonary Tuberculosis and to study the clinical profile and therapy of this association. The age of 40 years had Diabetes. Nanda and Tripathy (1968)[51] found prevelence of Diabetes in 12% of Tuberculous patients and stated that influence of Diabetes on Tuberculosis is as harmful as the impact of Tuberculosis on Diabetes and believed that tuberculous patients develop Diabetes probably more often than diabetic patients developing tuberculosis. Missing or overlooking the presence of Diabetes in Pulmonary Tuberculosis leads to disastrous culmination. With this in view the present study was undertaken to determine the incidence of Diabetes Mellitus in tuberculous patients admitted in Poona Chest Hospital, Aundh and to study the clinical profile and therapy of this association.

AIMS

The aims of the study were
1) To determine the incidence rate of the Diabetes Mellitus in Pulmonary Tuberculosis.

To study the clinical profile and therapy of this association.

To evaluate any other factors brought out during the course of study.

MATERIAL AND METHODS

Four hundred and forty consecutive patients of Pulmonary Tuberculosis admitted to the Poona Chest Hospital, Aundh during the period w.e.f. 1-7-91 to 30-6-92 comprised the material for this study.

After addmission in hospital, detailed history of present complaints with special reference to symptoms suggestive of Pulmonary Tuberculosis viz. cough, expectoration, haemoptysis, fever, night sweats, anorexia, weight loss, dysphonia, chest pain, malaise, weakness and symptoms suggestive of Diabetes Mellitus viz. polyuria, poly- dypsia, polyphagia, tingling and numbness, skin infections, visual symptoms etc. with duration, was taken in all cases. If the patient was a known case of Tuberculosis, detailed history about the treatment, duration of treatment and regularity of the treatment was recorded. Past history of Tuberculosis and family history of Diabetes Mellitus and Tuberculosis was noted.

The diagnosis of Tuberculosis was established by detailed clinical examination, bacteriological examination of the sputum and the radiological examination. Tuberculin testing, Pleural tapping (fluid report) and pleural biopsy (histopathological examination), Lymph node biopsy (histo- pathological examination), FNAB; Bronchoscopic aspirate and lavage for Acid fast bacilli were additive investigations for diagnosis in particular cases.

Sputum tests were done by sputum smear examination for identification of acid fast bacilli by the Ziehl-Neelson method of staining for three consecutive days by collecting 24 hours sputum and also by the culture of the sputum sample in Lowenstein-Jensen media. Chest X-rays were taken and extent of Tuberculosis was established by using criteria laid down by the National Tuberculosis Association of the U.S.A.[19]

1) Minimal lesion

Minimal lesions include those which are of slight to moderate density but which do not contain demonstrable cavitation. They may involve a small part of one or both lungs but the total extent, regardless of distribution should not exceed the volume of one lung on one side which is present above the second Costocondral junction anteriorly and the spine of the fourth or the body of the fifth thoracic vertebra posteriorly.

2) Moderately advanced

Moderately advanced lesions may be present in one or both lungs, but the total extent should not exceed the following limits:
Disseminated lesions of slight to moderate density which may extend throughout the total volume of one lung or the equivalent in both lungs; dense and confluent lesions which are limited in extent to one third the volume of one lung; the total diameter of cavitation if present must be less than 4 cms.

3) Far advanced

Lesions more extensive than moderately advanced.
Routine investigations, haemoglobin estimation, total and differential leucocyte counts, liver functions tests (eg.Bilirubin, Lever enzymes), blood urea and urine examinations were also done in each case before starting antituberculosis drug therapy.

The response to antitubercular treatment was judged by periodic check up of sputum examination for AFB (at least for two consecutive days after eight weeks and twenty six weeks) and also by periodic review of clinical and radiological status.

The patients so diagnosed as Pulmonary Tuberculosis were subjected for the diabetic status by detailed clinical history and investigations like - 1) Urine examination for presence of sugar by Benedict's test. Urine sample should be collected by double voiding method particularly for the morning sample so that the urinary glucose is more representative of the corresponding blood glucose. In double voiding method patient is instructed to void 30 minutes before obtaining urine for glucose determination.

Venous blood sugar level - Fasting over night and post-prandial by Follin-Ulu method.

Glucose tolerance test.

Criteria for Diagnosis of Diabetes

The National Diabetes Data Group of the National Institute of Health recommended relatively stringent criteria for establishing the diagnosis of Diabetes.[16] —

Fasting (overnight) venous plasma glucose concentration greater than 140 mg per decilitre on atleast two seperate occasions.

In the abesence of fasting hyperglycemia a diagnosis of diabetes can be made following ingestion of the standard 75 gram oral glucose tolerance test. If the two hour venous plasma glucose and one another sample (the 30",60",90" minute) exceed 200 mg per deciliter.

Impaired glucose tolerance exists if the fasting plasma glucose level is less than 140 mg per deciliter and if the 30", 60", 90" minute plasma glucose concentration exceeds 200 mg per deciliter along with a two hour plasma glucose level between 140 mg and 200 mg per deciliter.

The severity of diabetes was assessed by the levels of fasting blood sugar. A fasting blood sugar level of less than 150 mg% was graded as mild; 150-200 mg% of moderate and over 200 mg% as severe.[77]

Investigations included examination of the fundus, urine for albumin and ketone bodies, blood urea and electro-cardiograms. The response to antidiabetic treatment was

assessed by symptomatology of the patients and regular monitoring of urine and blood for sugar.

OBSERVATIONS

440 patients of Pulmonary Tuberculosis admitted to Poona Chest Hospital, Aundh, including males and females varying from 11 years to 75 years with the mean age of 43 years were studied for the spectrum of Diabetes Mellitus in Pulmonary Tuberculosis.

Table 2: Shows The Age And Sex Distribution Of Total 440 Patients Of Pulmonary Tuberculosis.

Sr.No.	Age	groups	male	female	Total	
1	11 -	20	20	21	41	
2	21 -	30	46	53	99	
3	31 -	40	50	20	70	
					210 (47)	.73
4	41 -	50	112	23	135	
5	51 -	60	55	17	72	
6	Above	60	15	8	23	
					230 (52	.27
TOTAL			298(67.73%)	142(32	*.27%*)440(100%)	

It was observed that amongst 440 cases of Pulmonary Tuberculosis 298 (67.73 percent) were males and 142 (32.27 percent) females. The male and female ratio was approximately 2=1. It was noticed that 210 cases (47.73 percent) were below the age of 40 years and 230 cases (52.27 percent) above the age of 40 years.

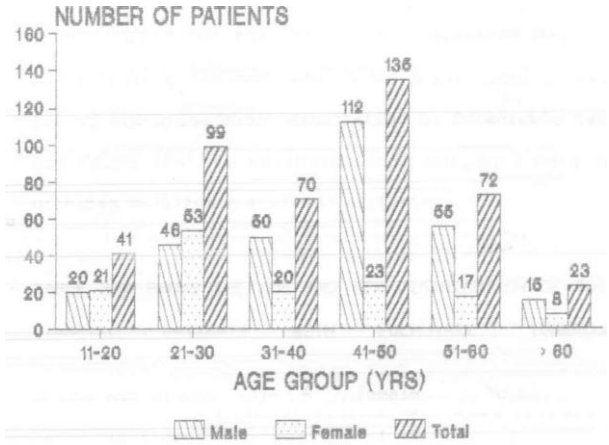


Fig 1: Age A Sex Distribution of Patient's of Pulmonary Tuberculosis.

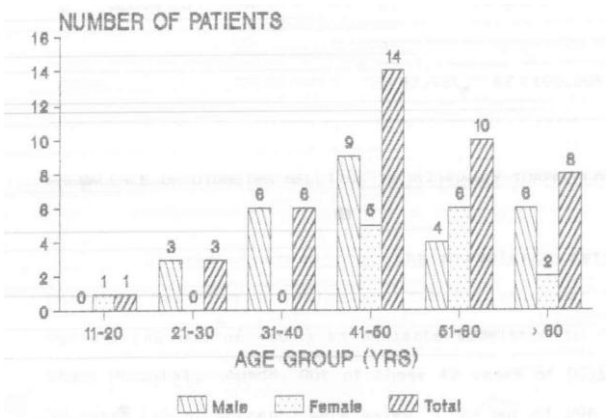


Fig 2: Age A Sex Distribution Of Patient Pulmonary Tuberculosis.

These 440 cases of Pulmonary Tuberculosis were investigated for incidence of Diabetes Mellitus by doing fasting and post meal blood sugar level by Folin-Wu method and urine sugar examination by Benedict's test. It was found that 42 patients (9.55 percent) were having Diabetes Mellitus out of 440 patients.

Table 3: Shows The Age And Sex Distribution Of Total 42 Diabetic Patients With Pulmonary Tuberculosis.

Sr.No.	Age	groups	male	female	Total	
1	11 -	20	—	1	1	
2	21 -	30	3	0	3	
3	31 -	40	6	0	6	
			9	1	10	(23.80 %)
4	41 -	50	9	5	14	
5	51 -	60	4	6	10	
6	Above	60	6	2	8	
			19	13	32	(76.20 %)
TOTAL			28(66.67%)	14(33.33%)	42	(100.00%)

Prevalence of Diabetes Mellitus In pulmonary tuberculosis

It was observed that the prevalence rate of Diabetes Mellitus in Pulmonary Tuberculosis was 9.55 percent (42 out of 440) in patients addmitted to Poona Chest Hospital, Aundh. Out of these 42 cases of Diabetes 1 cases (66.67 percent) were males (28 out of 298 male Tuberculosis patients) and 14 cases (33.33 percent) were

females (14 out of 142 female tuberculosis patients). 10 cases of Diabetes were below 40 years arid 32 patients of Diabetes were found to have Diabetes above 40 years.

Incidence of Diabettes Mellitus In Pulmonary Tuberculosis

Out of 42 patients of Diabetes 11 were known Diabetics including 6 males and 5 females and 31 were newly detected including 22 males and 9 females. So incidence of Diabetes Mellitus in patients of Pulmonary Tuberculosis admitted to Poona Chest Hospital, Aundh was 7.04 percent, as 31 new cases of diabetes were detected out of 440 patients of Tuberculosis and incidence rate of Diabetes amongst males was 7.38 percent (22 out of 298) and amongst females was 6.33 percent (9 out of 142). So it was observed that incidence in male was more than females. Below 40 years 2 cases of Diabetes were known out of 10, thus giving incidence of Diabetes in Pulmonary Tuberculosis as 3.80 percent (8 out of 210) below 40 years and above 40 years 9 cases were known out of 32, thus giving incidence rate of Diabetes Mellitus in Pulmonary Tuberculosis as 10.00 percent (23 out of 230) above the age of 40 years. So the incidence rate was markedly higher above 40 years of age. Amongst females only 1 case out of 14 female diabetics was below 40 years and 13 were above 40 years. So the frequency of Diabetes amongst females was also markedly higher above 40 years.

Table 4: Frequency of Symptoms of Pulmonary Tuberculosis In Non-Diabetic Patients.

Sr.No.	Symptoms	No.of cases	Percentage
1	Cough	350	87.94
2	Expectoration	316	79.39
3	Weight loss	313	78.62
4	Fever	304	76.38
5	Malaise	273	68.50
6	Anorexia	271	68.21
7	Weakness	227	57.03
8	Dyspnoea	205	51.31
9	Night sweats	149	37.43
10	Haemoptysis	124	31.15
11	Chest pain	84	21.01

It was observed that out of 398 Non-Diabetic Tuberculous patients frequency of haemoptysis was found in 124 cases(31.15 percent). Frequency of other symptoms include cough 350 cases (87.94 percent), expectoration 316 cases (79.39 percent), fever 304 cases (76.41 percent), night sweats 149 cases (37.43 percent), anorexia 271 cases (68.21 percent), weight loss 313 cases (78.62 percent), chest pain 84 cases (21.01 percent), malaise 273 cases (68.5 percent), weakness 227 cases (57.03 percent), and dyspnoea in 205 cases (51.31 percent).

Table 5: Shows Frequency of Symptoms of.

Sr.No.	Symptoms	No.of cases	Percentage
1	Cough	39	92.85
2	Expectoration	38	90.47
3	Fever	37	88.09
4	Weight Loss	33	78.57
5	Dyspnoea	32	76.19
6	Malaise	21	64.22
7	Haemoptysis	26	61.90
8	Weakness	23	54.71
9	Anorexia	19	44.20
10	Night sweats	15	35.70
11	Chest pain	09	21.91

Pulmonary Tuberculosis with Diabetes in 42 Cases.

It was observed that out of 42 patients of Non- Diabetic Tuberculosis frequency of haemoptysis was found in 26 cases (61.90 percent). Frequency of other symptoms include cough 39 cases (92.85percent), expectoration 38 cases (90.47 percent), fever 37 cases (88.09 percent), night sweats 15 cases (35.70 percent), anorexia 19 cases (44.20 percent), weight Loss 33 cases (78.57 percent), chest pain 9 cases (21.91 percent), malaise 21 cases (64.22 percent), weakness 23 cases (54.71 percent) and dyspnoea in 32 cases (76.19 percent). So freqency of heamoptysis in Diabetic Tuberculous patients was certainly higher (61.90 percent) as compared to Non-Diabetic Tuberculous patients (31.15 percent).

Table 6: Shows Frequency of Symptoms of Diabetes and Complication of Diabetes in Association With Tuberculosis.

Sr.No 1	Symptoms N< Polyur ia/Polydypsia	of cases 37	Perce 88	ntage.09
2	Weight Loss	26	61	.90
3	Tingling and Numbness	6	14	.2
4	Polyphagia	4	9	.52
5	Hypertension	3	7	.14
6	Skin Infection	2	4	.76
7	Visual Symptoms	2	4	.76
8	Hypoglycemic attacks	2	4	.76
9	Acetone in urine	2	4	.76
10	Urinary tract infection	1	2	.38
11	Ischamic heart disease	-		
12	Asymptomatic	3	7	.14

The above table shows that the classical symptoms of Diabetes like polyuria, polydypsia and weight loss were more common when the two diseases are associated. Polyphagia was infrequent because of the effect of Tuberculosis. Frequency of hypertension was 7.14 percent (3 out of 42 Diabetic patients) and tingling numbness in 14.2 percent cases.

RADIOLOGICAL FEATURES

1) Extent of Tuberculosis

Extent of Tuberculosis was established by using the criteria laid down by the National Tuberculous Association of U.S.A.

Table 7: Shows The Extent of Tuberculosis In Non-Diabetic Tuberculous Patients In 398 Cases.

Sr.No.	Extent of Tuberculosis	No.of cases	Percentage
=1=	Minimal	38	9.56
2	Moderately advanced	202	50.75
3	Far advanced	158 398	39.69 100.00

It was found that in 398 Non-Diabetic Tuberculous patients 38 cases (9.56 percent) had minimal lesions, 182 (50.75 percent) moderately advanced and 158 cases (39.69 percent) had far advanced Tuberculosis.

Table 8: Shows The Extents Of Tuberculosis In Diabetic Tuberculous Patients In 42 Cases.

Sr.No.	Extent of Tuberculosis	No.of cases	Percentage
1	Minimal	—	—
2	Moderately advanced	14	33.33
3	Far advanced	28	66.67

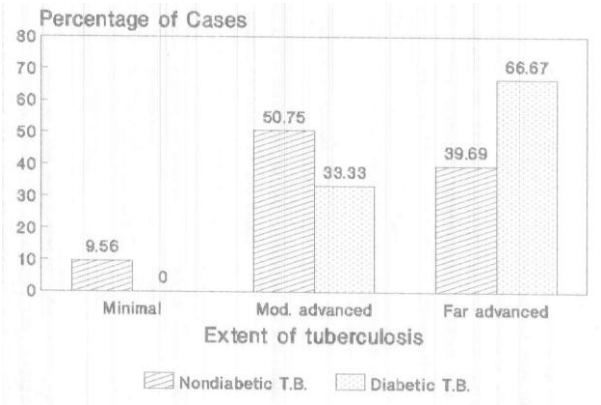


Fig 3: The Extent of Tuberculosis.

It was observed that in 42 patients of Diabetes Mellitus in association with Tuberculosis none had minimal lesions, 14 (33.33 percent) had moderately advanced lesions and 28 (67.67 percent) had far advanced diseases. This shows Diabetic Tuberculosis patients had more advanced lesions than non-Diabetic Tuberculous patients. (Fig.3).

2) Nature of Lesion

Table 9: Shows The Nature of Lesion In Non-Diabetic Tuber Culous Patients In 398 Cases.

Sr.No.	Nature of Lesion	No.of cases	Percentage
1	Exudative	89	22.36
2	Productive	168	42.22
3	Mixed(Fibrocaseous)	141	35.42
		398	100%

Out of 398 Non-Diabetic Tuberculous patients 89 cases (22.36 percent) had exudative, 168 (42.22 percent) productive and 141 (35.42 percent) had mixed (Fibrocaseaous lesions).

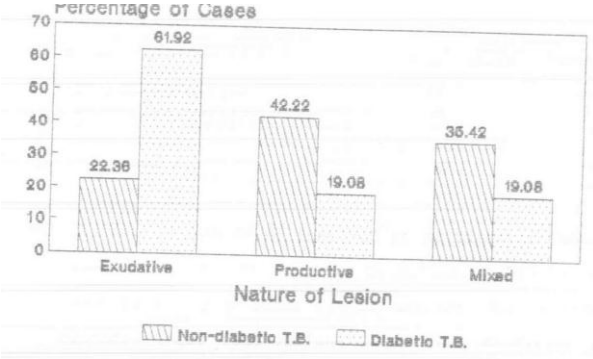


Fig 4: The Nature of Lesion.

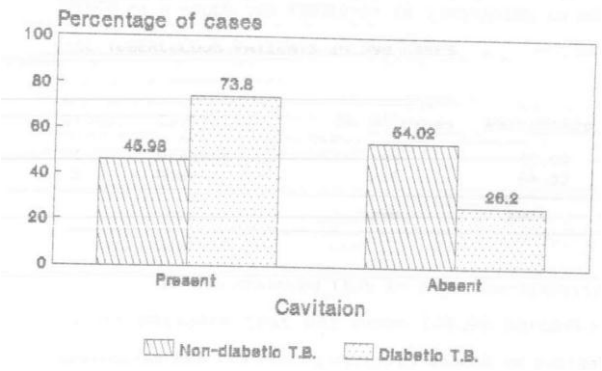


Fig 5; Frequency of Cavitation.

Table 10: Shows The Nature of Lesion In Diabetic Tuberculous Patients In 42 Cases.

Sr.No.	Nature of Lesion	No.of cases	Percentage
1	Exudative	26	61.92
2	Productive	8	19.04
3	Mixed(Fibrocaseous)	8	19.04
		42	100%

It was found that out of 42 Diabetic Tuberculous cases 26 (61.92 percent) had Exudative, 8 (19.04 percent) Productive and 8 cases (19.04 percent) had Fibrocaseous disease. These observations shows that exudative lesions were higher in frequency in Diabetics than in non-Diabetics. (Fig. 4)

3) Presence of Cavitation

Table 11: Shous The Frequency of Cavitation in Non-Diabe- Tic Tuberculous Patients in 398 Cases.

Sr.No.	Cavitation	No.of cases	Percentage
1	Present	183	45.98
2	Absent	215	54.02
		398	100%

It was observed that in 398 Non-Diabetic Tuberculous patients that 183 cases (45.98 percent) showed cavitation and 215 (54.02 percent) showed no cavitation.

Table 12: Shows The Freqency Of Cavitation In 42 Diabetic Tuberculous Patients.

Sr.No.	Cavitation	No.of cases	Percentage
1	Present	31	73.80
2	Absent	11	26.20
		42	100%

It was found that amongst 42 Diabetic Tuberculous cases 31 (73.80 percent) had cavitation and 11 (26.20 percent) had no cavitation. So it is observed that in Diabetics cavitation was more (73.8 percent) than non- diabetic tuberculous patients (45.98 percent). (Fig. 5) 4)

Diabetic Tuberculosis: Sosman and Steidl (1923)[73] had described " Diabetic Tuberculosis" having a specific radiological pattern. These lesions usually consists of a wedge shaped area of density in which there is often cavitation situated in the neighbourhood of hilum and spreading towards the periphery including the bases occur- ing in Diabetics over the age of 40 years. The lesions are usually acute, confluent and exudative.

Table 13: Frequency Of Radiological Pattern Of "Diabetic Tuberculosis" In 42 Patients Of Diabetes Associated With Tuberculosis.

Sr.No.	Sex	No.of cases	Percentage
1	Male	5	11.90
2	Female	2	4.76
	Total		16.66

It was observed that a specific radiological pattern called "Diabetic Tuberculosis" described by Sosman and Steid[7j] was found in 7 cases (16.66 percent) above 40 years of age in this combination disease. Out of these 7 cases 5 (11.90 percent) were in males and 2 (4.76 percent) were found to have in the females. (pig.7).

4) Site of the Lesion

Table 14: Shows The Site of Tuberculous Lesion in 398 Non-Diabetic Patients.

Sr.No.	Zones involved	No.of cases	Percentage
1	Upper	164	41.02
2	Middle	64	16.08
3	Lower	35	8.79
4	All Zones	137	34.12

It was observed that in 398 Non-Diabetic Tuberculous cases 164 (41.02 percent) had upper zone involvement, 64 (16.08 percent) middle zone involvement, 35 (8.79 percent) had lower zone involvement, and 137 cases (34.12 percent) all zones were involved.

Table 15: Shows The Site of Lesion In 42 Diabetic Tuberculous Patients.

Sr.No.	Zones involved	No.of cases	Percentage
	Upper Zone	5	11.90
	Middle Zone	8	19.05
	T-ower Zone	8	19.05
	All Zones	21	50.00
	100.00		

It was observed that in 42 Diabetic Tuberculous patients 5 cases (11.90 percent) had upper zone involvement, 8 (19.05 percent) middle zone involvement, 8 cases (19.05 percent) lower zone involvement, and in 21 cases (50.00 percent) all zones were involved. Thus it was found that in diabetic tuberculosis patients all zones were involved more (50 percent) as against non-diabetic (34.21 percent). Lower zone involvement in diabetics was considerably higher (19.05 percent) as against non-diabetics (8.79 percent) and middle zone involvement was also more.

5) Sideof Tuberculous Lesion

Table 16: Shows The Side of Tuberculous Lesion in 398.

NON- DIABETIC PATIENTS		
Sr.No.	Side of Lesion No.of cases	Percentage
1 2 3	Right 96 Left 73 Bilateral 229	24.12 18.35 57.35
	398	100.00

It was found that in 398 Non-Diabetic Tuberculous cases 96 (24.12 percent) had lesion on right side, 73(18.35 percent) on left side and 229 cases (57.35 percent) were with bilateral involvement.

Table 17: Shows The Side of Involvement In 42 Diabetic Tuberculous Patients.

Sr.No.	Side of Lesion	No.of cases	Percentage
1	Right side	7	16.67
2	Left side	5	11.90
3	Bilateral	30	71.43
		42	100.00

It was observed that out of 42 Diabetic patients associated with Pulmonary Tuberculosis 7 cases (16.67 percent) had lesion on right side, 5 (11.90 percent) on left side, 30 patients (71.43 percent) were with bilateral lesions. It was found that there was predilection for right side in these patients.

7. Severity of Diabetes Mellitus and Radiological extent

Table 18: Shows The Spectrum of Severity of Diabetes And Radiological Extent In 42 Diabetic Tuberculous Cases.

	Degree of Diabetes	Mellitus	Total
Radiological extent	Mild Moderate	Severe	
Minimal Moderately	9(21.42%)	5(11.9%)	14(33.33%)
Advanced Far Advanced	13(30.95%)	15(35.71%)	28(66.67%)
Total	22(52.38%)	20(47.62%)	42(100.0%)

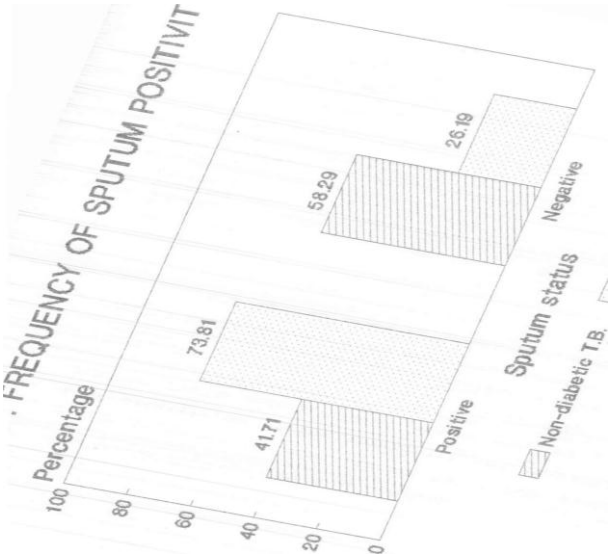
It was observed that out of 42 Diabetic Tuberculous cases 20(47.62 percent) had severe degree of Diabetes and 22(52.38 percent) cases were with moderate degree of Diabetes. Further, out of these 20 cases of severe Diabetes 15(35.71 percent) were having far advanced Tuberculosis and 5(11.9 percent) were with moderately advanced lesions. Out of above 22 cases of moderate Diabetes 13(13.95 percent) were having far advanced lesions and 9(21.42 percent) were with moderately advanced Tuberculosis. To summarize, 20 cases were with severe Diabetes and 28(66.67 percent) were with far advanced lesions, 22 cases were with moderate degree of Diabetes and 14(33.33 percent) were with moderately advanced Tuberculosis. Thus it shows that severity of Diabetes and Tuberculosis are interrelated as most of the cases were with moderate to severe Diabetes and with far advanced Tuberculosis. None was with mild Diabetes and minimal lesion.

BACTERIOLOGICAL SPECTRUM

Table 19: Shows Frequency of Sputum Positivity In Diabetes And Non- Diabetic Tuberculosis Patients.

Bacter io-logical	Diabetic tuberculous Cases		Non-diabetic tuber Culous Cases	
Status	No of Cases	Percentage	No of Cases	Percentage
Positive	31	73.81	166	41.71
Negative	11	26.19	232	58.29
Total	42	100.00	398	100.00

It was observed that out of 398 cases 166 (41.71 percent) of non diabetic tuberculosis were sputum positive and 232 (58.29 percent) were sputum negative. Out of 42 diabetic tuberculous cases 31 (73.81 percent) were sputum positive and 11 (26.19 percent) were sputum negative for acid fast bacilli. So it was observed that sputum positivity was markedly higher in diabetics (73.81 percent) than in non diabetic cases (41.71 percent). (Fig. 6).



TREATMENT AND FOLLOU UP

All cases of Pulmonary Tuberculosis with and without Diabetes Mellitus were treated with short course chemotherapy for 9 months as follows-

	DRUGS DOSAGE / SCHEDULE		PERIOD
	AS Per weight of	Commonly used	
	Patient(mg.per Kg.)	Doses	
1)	Isoniazid(H) 5 mg./kg.	300 mg. daily	9 months
2)	Rifampicin(R) lOmg./kg	450 mg. daily	9 months
		below 50 kg.wt.	
		600 mg. daily	
		above 50 Kg.wt.	
3)	Pyrazinamide 30-35mg./kg	1.5 gm daily	2 months
	(Z)	below 50 Kg.wt.	
		2 gm daily bet.	
		50 - 75 Kg wt.	
		2.5 gm daily	
		above 75 Kg wt.	
4)	Inj.Strepto- 15-20 mg./Kg	0.75-1 gm.daily	2 months
	-mycin (S) OR		
	Ethambutol 15-25 mg./Kg	600-800 mg.daily	2 months

In short 2 SHRZ + 7 HR or 2 EHRZ + 7 HR. Response to therapy was assessed by sputum conversion and radiological improvement.

A) Sputum Conversion

Table 21: Shows Bacteriological Conversion Of 31 Diabetic And 166 Non-Diabetic Patients (Sputum Smear Cum Culture Positive For Acid Fast Bacilli).

Months	Diabetic (total 31)		Non-diabetic (total 166)	
	No.	Percentage	No.	Percentage
2 Months	30	(96.77 %)	162	(96.98%)
3 Months	31	(100.00 %)	164	(98.79%)
4 Months	31	(100.00 %)	166	(100.00%)
6 Months	31	(100.00 %)	166	(100.00%)
9 Months	31	(100.00 %)	166	(100.00%)

It was observed that by the end of three months all the patients of Diabetes associated with Pulmonary Tuberculosis showed sputum conversion (100 percent) and bacterial quiscence was maintained till the end of sixth and nineth month. There was no significant variation in the rate of sputum conversion oberserved in two groups.

Follow-up of diabetic tuberculous patients was done up to 12 months after completion of therapy. Bacteriological relapses after stopping therapy was taken as two positive cultures of atleast 10 colonies obtained at different months in 3 consecutive months. None showed relapse within one year.

B) RADIOLOGICAL RESPONSE

Radiological improvement during therapy was observed as follows. (S.P. Agarwal et al (1985)

Slight: Resolution of lesion less than 25 percent of total involvement

Moderate: Resolution of lesion between 25 to 50 per-cent of total involvement.

Marked: Resolution of lesion more than 50 percent of involvement.

Cavity closure was also assesed for the radiological response to therapy.

It was observed that 40 out of 42 diabetic tuberculous patients show marked resolution by the end of 6 months of therapy. In spite of taking regular anti tuberculous therapy two patients required longer duration (15 months) of therapy as they were having poor control of diabetes due to irregularity in taking insulin. Subse-quently they were explained well for need of simultaneous therapy for both the diseases and responded well thereafter. One patient with Empyema and four patients of Pyopneumothorax of diabetic group needed intercostal drainage, subsequently with daily meticulous dressing and antibiotics showed complete resolution by the end of 9 months of therapy. Both the groups showed equally well radiological resolution and there was no significant variation among them.

One patient of Diabetes associated with Pulmonary Tuberculosis during treatment developed drug induced hepatitis. Rifampicin, Pyrazinamide and Isoniazid were withheld for a week and in the mean time continued with injection Streptomycin and Ethambutol. After clinical improvement and serum bilurubin and liver enzymes returning to normal, Isoniazid, Pyrazinamide and Rifampicin were seqentially introduced one by one by observing tolerance to the drugs.

ANTIDIABETIC THERAPY AND FOLLOW UP

In our study none was observed with mild Diabetes. Initially all the patients were treated with insulin along with anti-tuberculous therapy. As average insulin output of 70 kg man in 24 hours has been estimated to be 25 units, insulin therapy reasonably started with a total daily dose of 20 units per day with upward adjustment every several days based on the blood glucose level. After stabilization of Diabetes and finding out total requirement using soluble insulin in divided doses single daily injection of intermediate acting insulin [NPH (neutral protamine) or lente] was given. Because of post breakfast hyperglycemia observed in some cases it was necessary to mix it with short acting soluble (like in a single dose schedule instead of giving 25 units (TDD intermediate insulin, 20 units intermediate plus 5 units soluble insulin preferred). When the insulin requirement observed was more than 50 to 60 units it was given in two divided doses approximately two third in the morning and ane third in the evening of the total daily dose (TDD), the proportion of intermediate to rapid acting insulin at each injection was approximately two third to one third.

Oral anti-Diabetic drugs are classified as Sulfonylureas (eg. Tolbutamide, Tolazamide, Acetohexamide, Chlorpropamide (Diabinese), Glibenclamide (Euglucan), Glipizide) and Biguanide (Phenformin and Metformin). We have used mostly Sulfonylureas and Biguanides were less used as they show the side effect of lactic acidosis. When a patient of Diabetes on oral antidiabetic drugs is receiving Rifampicin,- since Rifampicin is a hepatic micro- zomal enzyme inducer and causes rapid metabolization of the oral antidiabetic drugs, therefore the dose of oral antidiabetic drugs has to be increased. After completion of the antitubercular therapy, the dose of oral antidiabetic drugs has to be reduced, otherwise the patient has chances of going into hypoglycemia.[8]

DIET

Diet containing 35 Kcal/kg/day in non obese or in most patients was given but upward or downward adjustments were made to achieve desired weight and requirement. 10-15 percent of total calories from proteins (1 gm per kg body weight), 50-55 percent calories from carbohydrates and 30-35 from fats (avoiding saturated fats) with essential nutrients comprised the diet. Neither liberal nor restricted strategy followed and diet was given as per requirement. Of the total calories distribution made as 20 percent for breakfast, 35 percent for lunch, 30 percent for dinner and 15 percent as a late evening feeding during antidiabetic therapy.

RESPONSE TO ANTIDIABETIC THERAPY

Response to anti diabetic therapy was assessed with urine glucose examination by collecting urine sample by double voiding method especially in the morning and periodic check up of blood glucose level. Titration of insulin requirement was solely made by oberving blood glucose level and not by urine glucose level as it gives a rough approximation of blood glucose level and modified by many factors like renal threshold, renal blood flow and volume of urine.

It was observed that 19 out of 42 diabetic patients initially required insulin more than 60 units daily. Out of these 19, by the end of 6 months requirement of 9 had come down to 50 - 60 units. Another 7 patients needed insulin 40 to 50 units daily initially out of which requirement of 4 came down to less than 40 units daily by the end of 6 months. 16 needed insulin less than 40 units daily in the beginning out of which 12 were switched over to oral anti-diabetic drugs by the end of third month. This shows that Tuberculosis acts as a stressful condition causing rise in blood sugar level. (Table: 22).

Table 22: Shows The Effect of Anti Tuberculous Therapy on The Requirement of Insulin.

Month	Requirement Of Total Insulin							Oral	Drugs
	(No. of patients)							(No.of	Pts.)
>60	units	50-	60	units	40-	50 units	<40	units	
First	19		0		7		16		0
Second	19		0		7		14		2
Third	17		2		6		1 + 11		5
Fourth	15		4		5		2+04		12
Fifth	13		6		4		3+04		12
Sixth	10		9		3		4+04		12
There	10		9		3		4+04		12
after									

PiScussIon

In the present study, 440 patients of Pulmonary Tuberculosis admitted to Poona Chest Hospital, Aundh were screened to find out the incidence rate of Diabetes Mellitus in Pulmonary Tuberculosis and to study the clinical profile of this association. The age of the patients varied from 11 years to 75 years with mean age 43 years. It was found that 230 patients (52.27 percent) were above the age of 40 years and 210 (47.73 percent) were below the age of 40 years. 142 patients were female (32.27 percent) and 298 (67.73 percent) were male giving male to female ratio approximately 2:1.

Incidence of Diabetes Mellitus In Pulmonary Tubercu L0sis

Out of 440 patients of Pulmonary Tuberculosis studied, it was observed that 42 had Diabetes Mellitus giving prevalence rate of Diabetes Mellitus of 9.55 percent in Pulmonary Tuberculosis. Out of these 42 Diabetics 1 were males and 14 were females; 10 were below 40 years and 32 were above 40 years. (Table 3, fig. 2).

Although, in the present study, 42 cases out of 440 were found to have Diabetes Mellitus in Pulmonary Tuberculosis, however, 11 cases (6 males and 5 females) were already known to be diabetics and 31 patients were newly detected. Thus in this study the incidence rate of Diabetes Mellitus in Pulmonary Tuberculosis was 7.04 percent. The incidence rate in males was 7.38 percent (22 out of 298) and in females 6.33 percent (9 out of 142).

Weiner and Kovee (1936)[83] reported that 6.4 percent of their 3385 Tuberculosis admissions had Tuberculo The overall prevalence of Diabetes in western general population is one percent (31). Prevalence of Diabetes Mellitus in general population in India is 1-2 percent as established by epidemiological studies.[58] A well recognised multi-centre study financed by the Indian Council of Medical Research (ICMR) showed that in persons over 15 years of age, the overall prevalence rate for India as a whole was 1.73 percent.[30]

Thus incidence rate of Diabetes Mellitus in patients of Pulmonary Tuberculosis admitted to Poona Chest Hospital, Aundh as 7.04 percent was significantly higher and concludes that Diabetes Mellitus does not exist in Pulmonary Tuberculosis merely by chance.

Brij Kishor et al (1973) in their study of 90 cases of Pulmonary Tuberculosis found Diabetes in 19 cases, of which 14 were males and 5 were females. A similar higher incidence in males has been reported by Lahiri and Sen (1974).[40] In addition, a peculiar finding noted by these workers was that females suffered less during

younger age but more after the age of 40 years. The frequency of Diabetes in Pulmonary Tuberculosis increases with the age of the patients (Turner Warwick, 1957[81], Kishore et al 1973, Lahiri and Sen 1974[40]).

Similar trend of Diabetes in Pulmonary Tuberculosis was observed in our study. Incidence rate of Diabetes Mellitus in Pulmonary Tuberculosis amongs males was 7.38 percent and females was 6.33 percent in our study which Nanda and Tripathy[51] also observed that out of 24 cases of Diabetes found out of 200 cases, 13 cases were with severe Diabetes and all were sputum positive; 8 were with moderate Diabetes and out of these eight, seven were sputum positive; only 3 were having mild Diabetes out of these three only one was sputum positive. This states that sputum positivity and severity of Diabetes are directly interrelated to each other.

In our study out of 42 Diabetic cases associated with Tuberculosis none was with mild Diabetes, 20 were with severe Diabetes and out of these 20 cases, 16 (80 percent) were sputum positive and 22 were with moderate degree Diabetes amongs which 15 (68.18 percent) were sputum positive (Table: 20). This gave the inference that sputum positivity and serverity of Diabetes are definitely interrelated to each other and thus also matching with the observations of Nanda and Tripathy.[51]

RADIOLOGICAL FEATURES OF ASSOCIATION OF DIABETES MELLITUS UITH PULMONARY TUBERCULOSIS

Extent of tuberculosis

Banyai and Cadden (1944) in their study of Tuberculosis patients complicated by Diabetes, 2.4 percent had minimal disease, 14.4 percent had moderately advanced disease and 83.2 percent had far advanced disease. Foley and Adosca (1944)[26] noted minimal lesion in none of the cases, moderately advanced in 39 percent and far advanced lesion in 61 percent cases amongst 28 Diabetic Tuberculosis patients. Boucot in 1952[13] also found the frequency of minimal lesions in 18.8 percent and advanced lesions in of Diabetic Tuberculosis patients 61.92 percent (26 cases) had exudative type lesion (8 cases) 19.04 percent each had productive and fibrocaceous lesion. Thus exudative type of lesions were significantly higher (61.92 percent) in Diabetics than in Non-Diabetics (22.36 percent) and were statistically highly significant ($P < 0.001$) (Fig. 4) So this corelates well with the observations made by other wor kers.

2) Presence of Cavitation

Banyai and Cadden (1944) observed that cavitory lesions are more common (71.2 percent) in patients of Diabetes Mellitus in association with Pulmonary Tuberculosis. Boucot (1952)[13] also noticed the incidence of cavitation more in Tuberculosis lesion of Diabetes than non- diabtic Tuberculosis patients.

Warwick M.T. (1957)[81] found in his study that 48 percent of Diabetic Tuberculosis patients had cavities. Brij Kishor et al (1973)[14] found the frequency of cavitation greater in manifest diabetes (75 percent) as compared to chemical group (66.7 percent) and in latent chemical Diabetes (33.3 percent) in his study of 90 patients of Pulmonary Tuberculosis for screening of Diabetes Mellitus by standard and prednisolone primes.

In the present study it was found that out of 42 patients of Tuberculosis associated with Diabetes 31 patients (73.80 percent) had cavitory lesions (Table : 12).

SITE OF TUBERCULOSIS LESION

Brij Kishor et al (1973), observed in patients of Diabetes associated with Pulmonary Tuberculosis that more often the lower zones were involved. Bhatia (1975)[12] observed 31.8 percent of his patients had a typical lesion like right middle lobe or lower zone involvement. Joseph T.Moris et al (1992)[34] described that Tuberculosis of the lower lung fields is most likely the result of trans-bronchial perforation of hilar node with spread to the adjucent lobe.

In the present study, it was observed that all zones were extensively involved in 21 cases out of 42 (50 percent) patients of Diabetes associated with Tuberculosis 19.05 percent (8 out of 42) of D.iabetic Tuberculosis patient had lower zone involvement as compared to 8.79 percent in Non-Diabetic Tuberculosis patients which was considerably significant. Middle zone in Diabetes shows 19.05 percent (8 out of 42) involvement giving more values compared to Non-Diabetic 16.08 percent (Table: 14 and 15).

Tuberculosis none had minimal lesion and mild Diabetes. 20 cases (47.62 percent) had severe Diabetes out of which 15 had far advanced Tuberculosis and 5 had moderately advanced Tuberculosis. 22 patients (52.38 percent) of Diabetic Tuberculosis had moderate Diabetes out of which 13 had far advanced and 9 were with moderately advanced Tuberculosis (Table: 18). Therefore we can conclude that severity of these diseases are interrelated.

Pulmonary Tuberculosis and Diabetes Mellitus often exist in association not merely by chance and when they do exist the prognosis is very grave. This is due to fact that early diagnosis of the association is very rare. By the time the diagnosis is made most of the cases have far advanced Tuberculosis and severe Diabetes. The main reason is that the symptoms of the complicating disease are masked by the originally existing disease. Further each condition causes exacerbation of the other. Moreover as both the diseases run a very chronic course patients are notoriously defaulters.

To reduce the mortality of this dreadful combination, effort should be taken to diagnose this combination as early as possible by doing routine blood sugar estimation

in Tuberculous patients particularly above the age of 40 years and carrying out routinely X-Ray exmination and sputum examinations in Diabetic patients and promptly treating them.

TREATMENT AND FOLLOW UP

Bhatia[11] felt that all patients of Diabetes associated with Tuberculosis should be hospitalised initially for stabilization of Diabetes. Tandon proposed that all the patients of Pulmonary Tuberculosis should be screened for Diabetes. Himsworth°[2] and Deshmukh[21] et al concluded that these patients do extremely well if properly treated for both the conditions. Brij Kishor et al observed 100 percent sputum conversion and during treatment the glucose tolerance test of all Diabetic patients showed a trend towards normalization. Patel J.C. et al[1] stressed that the physician should not fall a prey to the patients pleading for oral drugs in a situation where they are ineffective and insulin is the only alternative. Virendra Singh et al[78], Seth S.C. et al[71] and WHO study group on months for associated with impaired glucose tolerance test (In short 3 SHRZ + 6 HR for diabetic and 3 SHRZ + 3 HR for associated with impaired glucose tolerance).

In the present study we have treated with 9 months short term chemotherapy (2 SHRZ + 7 HR or 2 EHRZ +1 HR) in conventional doses for all the cases. Sputum conversion was 100 percent by the end of 3 months in diabetics and there was no significant variation in both the groups (diabetic and non-diabetic). All diabetics were kept in hospital till the stabilization of diabetes and initially treated with insulin. 40 patients of diabetes showed radiological resolution by the end of 9 months. Two diabetics needed longer duration of treatment (15 months) inspite of taking regular anti- tuberculosis therapy as they were having poor control of diabetes due to irregularity in taking insulin. After instructing well for the need of simultaneous treatment of both the diseases, Subsequently they responded well with control of diabetes and regular anti-tuberculosis therapy and cured. This shows cure of this association needs adequate therapy, overlooking one affects the fate of others and vice a versa. There was no significant variation in radiological resolution in the two groups.

Initially insulin requirement of 19 cases was 60 units out of which requirment of 9 had come down to 50-60 units, 7 cases requiring 40-50 units of insulin in the beginning, requirement of 4 of these came down to below 40 units by the end of 6 months. 16 cases were requiring insulin less than 40 units initially, 12 out of them were switched over to oral hypoglycemic drugs by the end of 3 months after observing the response to the oral drugs. Those who needed only insulin for control of diabetes were continued with insulin. Thus there was a downward trend of insulin requirement by the end of 6 months and this shows that tuberculosis infection certainly contributes to the rise in blood sugar level and matches with the observation made by the others. Patients treated with anti-tuberculo- sis drugs with proper control of Diabetes show extremely good response.

SUMMAR-Y AND CONCLUSIONS

Tuberculosis is a chronic bacterial infection caused by Mycobacterium tuberculosis and charecterised by the formation of granulomas in infected tissues and by florid cell-mediated hypersensitivity. The usual site of the disease is the lungs, but other organs may be involved. In the absence of effective treatment, a chronic wasting course is usual and death ultimately supervenes in most cases.[10]

Diabetes Mellitus is a heterogenous primary disorder of carbohydrate metabolism with multiple etiologic factors that generally involve absolute or relative insulin deficiency or insulin resistance or both. All causes of Diabetes ultimately lead to hyperglycemia, which is the hallmark of this disease syndrome.[16]

Diabetes Mellitus and Pulmonary Tuberculosis are major killers of mankind since ages back. The seriousness of this association of Pulmonary Tuberculosis and Diabetes Mellitus was first noted by the great Arab physician Avicenna[1] nearly 1000 years ago. In the past it was generally believed that the Tuberculosis was the complication of Diabetes and this association of Pulmonary Tuberculosis was thought to be one sided. Root and Dickson[66] stated that Tuberculosis patients do not develop Diabetes with any greater frequency than Non-Tuberculous. The converse relationship i.e. that patients with Tuberculosis have a high prevalence of Diabetes was until the 1950's less widely accepted. Nichols (1957)[53] in his study found evidence of glucose intolerance using an oral glucose tolerance test in 22 percent of 178 subjects with Tuberculosis and 5 percent had Diabetes. Since that time most of the studies have shown that the prevalence of Diabetes is indeed greater in patients with Tuberculosis. Deshmukh M.D.[1] in his study found 14 percent of tuberculous patients above the age of 40 years had Diabetes. Nanda and Tripathy[51] found prevalence of Diabetes in 12 percent of tuberculous patients and stated that influence of Diabetes Incidence rate of Diabetes in Pulmonary Tuberculosis amongst patients admitted to Poona Chest Hospital, Aundh was 7.04 percent which is higher than general population. Incidence rate amongst males was 7.38 percent and females it was 6.33 percent, above 40 years it was 10 percent and 3.8 percent below 40 years. So the incidence rate was more above 40 years of age and amongst males.

Frequency of haemoptysis and sputum positivity was higher in diabetics than non diabetics which was statistically significant.

Far advanced lesions, exudative lesions cavita- tive lesions were higher in frequency in diabetics than non diabetics and were statistically significant.

Diabetic Tuberculosis - the specific radiological pattern was observed in seven diabetics (16.66 percent) In our study none was with mild Diabetes and minimal lesion on radiography. Sputum positivity for acid fast bacilli and far advanced lesions were with higher frequency in patients with severe degree of Diabetes than moderate Diabetes.

When treated with anti-Tuberculosis short course chemotherapy and insulin, all patients responded extremel- ly well, showed good radiological resolution and 100 percent sputum conversion.

By the end of six months of therapy majority showed decreased requirement of insulin and 12 requiring insulin were switched over to oral antidiabetic drugs after observing the response. This shows the stress of tuberculous infection is certainly a contributory factor in raising blood sugar level and thus the increased in- cidence rate.

CONCLUSIONS

Since an association between Diabetes and Pulmonary Tuberculosis has already been described, all patients of Pulmonary Tuberculosis should be screened for presence of Diabetes especially those above 40 years of age.

The diagnosis of the Diabetes should be considered in patients of Pulmonary Tuberculosis who do not respond as expected to anti-Tuberculosis therapy, and also those who complain of exessive fatigue, polyuria, polydyp- sia and any who have evidence of diabetic complications such as paraesthesia or soft tissue infections.

Patients with lower lung field Tuberculosis should be investigated to rule out Diabetes.

Pulmonary Tuberculosis should be suspected in a Diabetic with an abnormality on chest roentgenogram.

In any Diabetic yearly sputum and x-ray examination or any occasion when cough persists for a month or so, if insulin requirement suddenly goes up, should be done to rule out Pulmonary Tuberculosis.

All patients of Diabetes associated with Tuberculosis should be hospitalised for stabilisation of Diabetes.

440 consecutive patients of Pulmonary Tuberculosis admitted to Poona Chest Hospital, Aundh w.e.f. 1-7 91 to 30-6-92 varying from 11 years to 75 years with mean age of 43 years were screened for Diabetes. Among these 298 were males and 142 females. A total number of 42 Diabetes were found in this series out of which 11 were known diabetics (6 males and 5 females) and 31 newly detected.

All patients should be vigorously and simultaneously trreated with anti- tubercuolsis therapy and insulin. At least insulin should be given initially till the Diabetes is stabilised. The physician should not fall a prey to the patients pleading for oral drugs in a situation where they are ineffective and where insulin is the only alternative.

Titration of insulin should be assessed by observing blood glocose level rather than urine glucose level.

Rifampicin is a hepatic microzomal enzyme inducer and causes rapid metabolisation of anti-Diabetic drugs. Therefore the dose of oral anti-Diabetic drugs may need to be adjusted when given concomittantly with Rifampicin and when patient is off Rifampicin.

We infer that short course anti-tubercuiar chemotherapy is highly effective in the management of Pulmonary Tuberculosis with Diabetes provided that the blood sugar level is adequately maintained throughout the duration of the treatment.

Six to twelve months after stoppage of therapy patient should be reviewed for diabetic status, as many patients show trend towards normalisation of blood sugar level after cure of Tuberculosis.

BIBLIQGRAPHY

1. Avicenna: Text book of Tuberculosis Eds., in chapter Tuberculosis inrelation to Diabetes by Deshmukh M.D., 1981; 252.
2. Agarwal S.K., Roy D.C., Sunder S., Metah N.C.: Short course intermittent Chemotherapy. J.A.P.I., 1985; 33: 4: 281.
3. Aretaeus (First century A.D): A.P.I. Text Book of Medicine, Eds., in chapter Diabetes Mellitus by B.B. Tripathy, 1988; 246.
4. Beinyai A.L. and Cadden A.V.: Arch. Int. Med., 1944; 74: 445-56.
5. Betnyai A.L.: Dis. Chest, 1959; 36: 238.
6. Bahl A.L.: Complication of Diabetes Mellitus, J. Ind. Med. Asso. 1968; 50: 195-98.
7. Bahulkar and Lokhandwala: Text Book of Tuberculosis by K.N. Rao Eds. in chapter Tuberculosis in relation to Diabetes by Deshmukh M.D., 1981; 252.
8. Bell: In Joslins Diabetes Mellitus, 9 th Eds. Lea & Febiger, Philadelphia, 1952.
9. Benjamin P.V. and Verghese M.C.: Pulmonary Tuberculosis and Diabetes Mellitus. Ind. Med. Gaz, 1940; 75: 588-90.
10. Best and Banting (1927): In Joslin's Diabetes Melli- tus, Lea and Febiger, Philadelphia, 12th edition, 1985; 380.
11. Bhatia J.L.: Pulmonary Tuberculosis with Diabetes Mellitus, Proceedings of the 18th Tuberculosis and chest diesease worker's conference, 1962; 326.
12. Bhatia J.L.: Text book of Tuberculosis by K.N. Rao, Eds. 1981; in chapter Tuberculosis in relation to Diebetes by Deshmukh M.D., 1975; 252-257.
13. Boucot K.R., Kooper D.A., Dillon E.S., Meier P and Richardson R.: tuberculosis Among Diabetics: The

Philadelphia Survey. Ame. Rev. Tub., 1952; 65(1): 1-50.
14. Brij Kishore, Nagrath S.P., Mathur K.S., Hazra D.K. and Agrawal B.D.: Manifest, Chemical and Latent Chemical Diabetes in Pulmonary Tuberculosis. J.Asso. Phys. Ind., 1973; 21: 875-880.
15. Charaka and sushruta (600-400 B.C.) Joslin's Diabetes Mellitus 12th Eds. 1985 published by Lea and Febiger, Pheiladelphia.
16. Cecil Text Book of Medicine 18th Eds. 1988 in Chapter Diabetes Mellitus by Jerroid M. Olefsky.
17. Cheung: Joslin's Diabetes Mellitus, 11th Eds. Lea and Febiger, Philadelphia, 1962; 630.
18. Claud Bernard(1850): A.P.I. Text Book of Medicine, Eds.; in chapter Diabetes Mellitus by B.B.Tri- pathy, 1988; 246.
19. Crofton and Douglas's Respiratory Diseases: Eds.1990; National Tuberculosis Association of U.S.A. Diagnostic Standards and classification of Tuberculosis. National Tuberculosis Association, New York, 1961.
20. Datta Choudhary A. and Mitra S.K.: Surgical treatment of Pulmonary Tuberculosis associated with Diabetes Mellitus. J.I.M.A., 1964; 43: 260.
21. Deshmukh M.D., Master T.B., David J.C. and Tripathy S. Jr. J.J. Group of Hospital and G.M.C. 1966; 2: 97-102.
22. Deshmukh M.D.: Tuberculosis in relation to diabetes in Text Book of Tuberculosis Edited by K.N. Rao 2nd Eds. 1981, 253-258.
23. Deshmukh M.D.: Tuberculosis and Diabetes Ind. J. Tub.1984; 31: 107-8.
24. Dingley H.B.(1966): Proceedings of the 24th Tubercu
25. losis and Chest Disease Conference, Trivedrum, Jan. 1969, P.350.
26. Ferrara M.A.: The Tuberculosis in Diabetic patient New England J.Med. 1952; 55,246
27. Foley J.A. and Adosca J.B.: Med. Clin. N. Amer. March 1944, 499.
28. Franke and Fuchs: Joslin's Diabetes Mellitus Leo and Febiger 12th Eds. 1985; in chapter Oral Hypoglycemic Agents, 1955; 412.
29. Golden R. (1927): Quoted by Banyayi and Caddn Arch. Int. Med., 1944; 74: 446-56.
30. Grafe E.: Metabolic Diseases and their treatment, Philadelphia, Lea and Febiger, 1933.
31. Gupta 0.P.et al (1984): Diabetes Mellitus in develop ing countries, J.S.Bajaj et al (Eds.). Interprint New Delhi quoted by J.E.Park in Text Book of Preventive and Social Medicine 12th Eda 1989; 252.
32. Harrison's Text Book of Principles of Internal Medi- cine 12th Eds., 1991.
33. Himsworth H.P.: Quart. J. of Med., 1938; 7: 373.
34. Israel H.L. and Payne H.M.: Amer. Rev. Tuber, 1940; 41: 188.
35. Joseph T. Morris, Maj. M.C., Barbara J. Seaworth M.O. and C. Kenneth, M.C. Allister. chest., 1992; 102(2): 539-41.
36. Joslin E.P.: Joslin's Diabetes Mellitus Edited by Marble A., White P., Branley R.F. Krall L.P., 11th Eds. (Indian Eds.). Published by Lea and Febiger, 1934; 621-636.
37. Joslin E.P. Joslin's Diabetes Mellitus 11th Eds, 1971; 628.
38. Keeton R.W.: Cited by Rest, Amer. Rev. Tubr, 1941; 43: 344.
39. Khanna B.K.: pulmonary Tuberculosis and Diabetes Mellitus J. Ind. M. Ass., 1968; 50: 407-413.
40. Kurzrock M., Anderson P.: Quoted by Boucot et al Amer. Rev. Tuber, 1952; 16.
41. Lahiri D.C., Sen P.K. Ind. J. of Tuberc, 1974; 21: 98.
42. Landis, Funk and Mongomery: Amer. Rev. Tuber, 1919; 2: 690.
43. Lieutaud (1779) and John Rollo: Text book of Tuberculosis by K.N.Rao Eds.1981 in chapter Tubercu -losis in relation to Diabetes by Deshmukh M.D., 1798; 252-257.
44. Long E.R.: Amer. Rev. Tuberc, 1930; 22: 567.
45. Luntz Grwn: The Prognosis of Tuberculosis in Diabetic Patients. Tubercle, 1961; 42: 375-78.
46. Malins J.: Clinical Diabetes Mellitus, 1st edition (1968) published by Fyre and Spottis UJood, London.
47. Marais: S.Afr. Med. J., 1980; 57: 483-484.
48. Moen J.K. and Reimann: Arch. Int. Med., 1933; 51: 789.
49. Moolten S.E.: Arch. Int. Med., 1940; 66: 561.
50. Mugusi F., Swai A.B.M., Alberti G.M.M. and McLarty D.G.: Increased Prevalence of Diabetes Mellitus in patients with Pulmonary Tuberculosis in Tanzania. Tubercle, 1990; 71: 271-276.
51. Mukherjee A.B., Sen S., Dey P.: J. Ind. Med. Asso, 1973; *6: 21*.
52. Nanda C.N., Tripathy S.N.: Association of Diabetes Mellitus with Pulmonary Tuberculosis. J. Asso. Phys. Ind., 1968; 16: 741-746.
53. Neogi B.P. and Roy K.S.: J. I. M. A., 1944; 13: 243.
54. Nichols: Diabetes among Young Tubercular patients, Review of the Association of two diseases. Amer. Rev. Resp. Dis., 1957; 76: 1016.
55. Opie (1819): A.P.I. Text Book of Medicine, Eds., in chapter Diabetes Mellitus by B.B. Tripathy, 1988; 246.
56. Oluboyo P.O. and Erasmus R.T.: The Significance of glucose intolerance in Pulmonary Tuberculosis. Tuber cle, 1990; 71: 135-138.
57. Patel A.G.: Text Book of Tuberculosis by K.N., 1975.
58. Rao. Eds. in chapter Tuberculosis in relation to Diabetes by Deshmukh M.D., 1981; 252-257.
59. Patel J.C., De Souza, Cheryl and Jigini S.S.,: Dia - betes and Tuberculosis, Ind. J. Tuber, 1977; 24: 155-158.
60. Park J.E. (Text Book of Preventive and Social Medi- cine 12th Eds, 1989.
61. Ralli and Steinberg: J. Lab. Clin. Med., 1938; 23: 581.

62. Rao K.N.: Text Book of Tuberculosis Eds., 1981.
63. Rathery R., Marrie J. and Roy: Quoted by Benyayi Cadden: Arch. Int. Med., 1944; 74: 445-56.
64. Reaud A.: Diabetes and Tuberculosis. South M.J., 1953; 46: 148.
65. Rest A.: Tuberculosis in Jewish Diabetics, Amer. Rev. Tuber, 1941; 43: 344.
66. Root H.F.: New Eng. J. Med., 1934; 210: 1.
67. Root H.F. and Bloor W.R.: Amer. Rev. Tuberc, 1939; 39: 714.
68. Root H.F. and Dickson R.: Joslin's treatment of Dia betes Mellitus, Chapter 22, Lea and Febiger, Phila delphia, 1952.
69. Root H.F.: Joslin E.P. Treatment of Diabetes Melli tus, Lea and Febiger, Philadelphia, 1952.
70. Ross and Home: Modern Drug Treatment of Tuberculosis Indian Eds, 1992.
71. Ross J.D.: Diabetes and Tuberculosis. Tubercle, 1973; 54: 132-133.
72. Roychowdhury A.B. and Sen P.K.: Diabetes in Pulmonary Tuberculosis J.I.M.A., 1980; 74: 8-13.
73. Seth S.C., Parmar M.S., Saini A.S., Harbans L.: Glucose tolerence in Pulmonary Tuberculosis. Horm. Metab, 1982; 14: 50.
74. Simonin R., Charpen J., Arhesser P. and Luciani J.M.: Ann. Endocr, 1966; 27: 261.
75. Sosman and Steidl: Amer. J. of Roentgenology, 1927; 17: 525.
76. Steinbach M.M., Klein S.J. and Deskowitz M. Amer. Rev. Tuber, 1935; 32: 665.
77. Tripathy S.R., Kar K. P. Chaudhary D.C. and Mujamdar K.: Ind. J. Tub., 1984; 31: 122-125.
78. Tullock J.A.: Diabetes Mellitus in the topics, E.&S. Livingstone, London, 1962; 131.
79. Vigg Bansilal, Sahay, Binod Kumar and Prabhakarlingam: J.A. P.1. 1971; 19: 843-849.
80. ^irendra Singh, Goyal R.K., Mathur M.N.: Glucose intolerence in patients with Pulmonary Tuberculosis. J.I.M.A., 1978; 70: 81-83.
81. Vrhovac V. (1937): Quoted by Banyai and Cadden Arch. Int. Med., 1944; 74: 445-56.
82. Von Mering and Minkowsky (1889) A.P.I.Text Book of Medicine Eds. In chapter Diabetes Mellitus by B.Tripathy, 1988; 246.
83. Uarwick M.T.: Pulmonary Tuberculosis and Diabetes Mellitus. Quart. J. Med., 1957; 26: 36-41.
84. Weaver R.A.: Unusal Radiographic Representation of Pulmonary Tuberculosis in Diabetic patients. Amer. Rev. Resp. Dis., 1974; 109: 302-308.
85. Weiner J.J and Kovee: Pulmonary Tuberculosis and Diabetes Mellitus. Amer. Rev. Tuber, 1936; 34: 179.
86. Zack M. D., Fulkerson L.L., Stein B.: Amer. Rev. Resp. Dis., 1973; 108: 1164-1169.