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A STUDY OF CLINICAL SPECTRUM OF TUBERCULOSIS IN DIABETES MELLITUS AND ITS RELATIONSHIP WITH GLYCEMIC STATUS IN TERTIARY CARE HOSPITAL, MYSORE

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BACKGROUND:

Tuberculosis is one of the deadliest communicable diseases in the world. Diabetes mellitus (DM) is recognised as an important risk factor for tuberculosis (TB). India has high-TB burden, along with rising DM prevalence.

AIM:

This study was conducted to document the co-existence of DM and TB in persons with established TB and difference in clinical presentation and to study the radiological features of pulmonary TB in diabetic patient.

MATERIALS AND METHODS:

The study was conducted on patients with diagnosed with TB and diabetes mellitus, admitted to K R hospital, Mysuru. This was a cross-sectional study conducted over a period of January 2020 to Dec 2020

RESULTS:

In our study, majority of the patients were in age group of 35-50 years and mean age was 42.2 years. Out of 100 people 77 were males and 23 were females. Most common manifestation of TB among diabetes patients is pulmonary TB [68%]. The incidence of extra-pulmonary TB was 32%, pleural TB being most common .In chest x-ray studies, bilateral lower zone involvement was more common [67.9%] in patients with poorly controlled blood sugars.

CONCLUSIONS:

In this study, the common manifestation of TB in diabetic patient was pulmonary TB with atypical chest x-ray findings i.e., lower zone or multi zone involvement which was associated with poor glycaemic control. Among group with poor glycaemic control [hba1c>10%], the most common extra-pulmonary manifestation of TB is disseminated TB and TB lymphadenopathy followed by bone TB. The most common extra-pulmonary manifestation seen among diabetic patients overall was pleural TB, which was most frequently seen with well controlled and

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moderately controlled diabetes and was absent in poorly controlled diabetes. TB lymphadenopathy was the second common extra-pulmonary manifestation TB. Although the severity and manifestation of TB is effected by glycaemic status, the incidence of drug resistant TB is lesser among diabetic people as per this study

INTRODUCTION

Tuberculosis is one of the deadliest communicable diseases in the world with estimated 9 million cases, with India alone accounting for 2.79 million cases.[1]Prevalence of diabetes mellitus in India ranges from 8.3%-12.4%[2,3],10% cases of tuberculosis are linked to diabetes mellitus.[1,4]

Diabetes and tuberculosis complicate each other at many levels – chances of relapse, treatment failure, mortality, delayed mycobacterial clearance[5,6,7,8].The rising prevalence of DM in high in TB burden countries like India, may adversely affect TB control[1], Diabetes Mellitus (DM) almost triples the risk of developing tuberculosis (TB)[2]. According to the World Health Organization (WHO), 180 million people are suffering from diabetes worldwide, and it is likely to double in the next 10 years, i.e., by 2030 [1]

The relationship between DM and pulmonary TB has attracted the interest of many clinicians and investigators for a long time. Many studies have shown that the prevalence of TB among diabetics is 2–5 times higher than in the non-diabetic population.[6] Concomitant TB and DM is associated with more severe features of TB including increased lung cavitations, increased involvement of lower lung fields and longer periods of smear positivity[9].The probable reason being, DM causes immune dysfunction and moderate suppression of the immune system. Reduced T-helper1 (Th1) cytokine response level is also seen amongst diabetic individuals. This immune dysfunction is detrimental to the immune response against TB. Th1 cytokines are vital in the control and inhibition of TB bacillus.[10,11]

Also, the degree of hyperglycemia has been found to have a distinct influence on the microbicidal function of macrophages, with even brief exposures to blood sugar level of 200 mg% significantly depressing the respiratory burst of these cells[11,12] .Chronic hyperglycemia causes non-enzymatic glycation of the chest wall and bronchial tree collagen protein that leads to fibrous tissue formation. Due to increased protein catabolism, there is decreased respiratory muscle strength, neuropathy of phrenic nerve may cause diaphragmatic paralysis. So, the diabetes mellitus causes reduced ventilatory function. The disease also causes thickening of the basal lamina by glycation and reduces the gas diffusing capacity. Hyperglycemia reduces antioxidant functions of lungs, local oxidative stress reduces the lung volumes, elastic recoil of the lungs and also causes reduced bronchodilatation

Lung dysfunctions in diabetes remain clinically silent for a long time because alveolar-capillary system of the lungs is characterized by a great micro vascular reserve. So it compensates for a decline in lung functions[10]. But loss of micro vascular reserves in lungs may become clinically important under stressful conditions like asthma, pneumonia or fluid overload secondary to heart failure. Decreased mobilization of polymorphonuclear leukocytes, chemotaxis, and phagocytic activity may occur during hyperglycemia[13,14,15,16]

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TB-DM patients are less likely to present with extra-pulmonary TB[17,18,19,20]. This may be due to a hyper-reactive cell-mediated immune response to M.TB in DM patients that may be suboptimal for containing M.TB growth within the lung, but effective for preventing its dissemination and reactivation elsewhere[21,22]. With the following rationale in mind, this study was conducted to estimate the prevalence of impaired TB both pulmonary and extra-pulmonary TB in patients with diabetes and to determine various study variables and clinical factors that may be associated with the same retrospectively.

MATERIALS AND METHODS: This study was a cross-sectional study conducted at a tertiary care hospital during the period 1stJanuary 2020 to 31stDecember 2020. Sample size was taken as 100 [ref. Prevalence of diabetics among tb patients in urban health centre, Ahmedabad by Sahil Mansuri et.al in july 2015(23)] Institutional ethical committee clearance taken[MMCRI/IEC/115/2019] and informed consent obtained from the study participants.

INCLUSION CRITERIA: Patients with diabetes mellitus diagnosed with either pulmonary or extra pulmonary tuberculosis and age >18years

EXCLUSION CRITERIA**:** Patients having any other respiratory illness not related to pulmonary TB,Patients having any other systemic diseases, Pregnant women, Patients with known immunocompromised status

`The participants were clearly explained about the objectives of the study and informed consent was obtained in local language (kannada) prior to administration of the interview schedule.

All participants fulfilling the inclusion criteria were interviewed as perproforma which included the demographic details, chief complaints, clinical examination details, blood investigations (Complete blood count & ESR,FBS & PPBS,HBA1C,RFT ,LFT,HIV,HBSAg) Sputum AFB ,CBNAAT ,Chest xray;IF RELEVENT-Plueral fluid analysis,Ascitic fluid analysis ,FNAC lymph node,Excisional biopsy lymph node,USG abdomen,CECT abdomen,X-ray spine AP & lateral,MRI whole spine screening, CT brain. The diagnostic probability was based on clinical data obtained from the patient charts and the results of relevant investigations. Data obtained from these patients were systematically recorded and analyzed using Statistical Package.

Statistical analysis

Data was analyzed using frequency proportion and relationship with glycemic status was analysed using chi square test for proportion and The results were analysed using the SPSS software 16th version. All the results were expressed as Mean ± SD.

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RESULTS

OBSERVATION AND ANALYSIS

TABLE :1 -Demographic Distrubution : The majority of the population in the study belonged to the age group of 36-50(52%) followed by 50 plus (39%) . The study population had the male female ratio of 3.3:1, Majority of male population belonged to the age group of 36-50 years (50.6%), so was female study population (56.5%)

Age group(years)	No.(percentage)
<35	9(9%)
36-50	52(52%)
50+	39(39%)
Total	100(100%)
SEX	
Males	77(77%)
Females	23(23%)

TABLE 2: Pulmonary vs extra-pulmonary tuberculosis
The most common presentation of tuberculosis in diabetic patient was pulmonary TB which was about 68%

	NUMBER	PERCENTAGE
PULMONARY TB	68	68%
EXTRA-PULMONARY TB	32	32%

TABLE 3: Distribution Of Extra-Pulmonary Tb

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The most frequent extra-pulmonary presentation in diabetic patients in this study was found to be pleural tuberculosis [31.2%] followed by tubercular lymphadenopathy [28.1%]

EXTRA-PULMONARY TB	NUMBER	PERCENTAGE
ABDOMINAL TB	3	9.3%
PLEURAL TB	10	31.2%
TB LYMPHADENOPATHY	9	28.1%
CNS TB	3	9.3%
TB BONE	3	9.3%
DISSEMINATED TB	4	12.5%
	32	100%

TABLE 4: Incidence Of Extra-Pulmonary Tb With Respect To Glycemic Control [Hbaic]

In this study most of the extra-pulmonary TB [53.1%] fall under the category of moderately controlled diabetes

EXTRA-PULMONARY TB	HBAIC <7.5%	HBA1C 7.5% - 10%	HBA1C >10%	PERCENTAGE %
ABDOMINAL TB	_	3	_	9.3%
PLEURAL TB	5	5	_	31.25%
CNS TB	2	1	_	9.3%
BONE TB	_	1	2	9.3%
TB LYMPHADENOPATHY	_	6	3	28.12%
DISSEMINATED TB	_	1	3	9.3%
TOTAL	7	17	8	32
PERCENTAGE	21.8%	53.1%	25%	100%

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PULMONARY TUBERCULOSIS:

TABLE 5: HbA1c V/S Sputum AFB Postivity , CBNAAT and Chest Xray involvement

From table 5, it is inferred that people with poor diabetic control had sputum infectivity [3+] , most of the diabetic patients had lesser incidence of resistant TB although patients with resistant TB [8.8%] had poorly controlled diabetes and moderately and poorly controlled sugars had increased incidence of lower zone opacities [64.7%].

Sputum AFB	HbA1C(%)			Total
	<7.5	7.5-10	>10	
1+	5	6	1	12
2+	2	16	6	24
3+	0	11	21	32
CBNAAT				
Rifampicin Resistant	0	3	3	6
Rifampicin sensitive	7	30	25	62
CHEST XRAY				
Upper zone	7	13	3	23
Bilateral upper zone	0	1	0	1
Lower zone+/- middle zone	0	11	6	17
Bilateral Lower zone/multizone	0	8	19	27

DISCUSSION

In this study out of 100 people studied, 77% are males and 23% were females, this is comparable to study by **Anil Kumar Agarwala** et al[24], where 77% were males and 22% were females and also comparable to study by **Patil Shital** et al[25] where 77.5% were males and 23.5% were females

Most of the people [52%] were in the age group between 35-50 years with mean age being 42.2 years, this is comparable to study by **Anil Kumar Agarwala**et al where mean age was 43.4 years

Comparision of incidence of pulmonary tb with other authors: Incidence of pulmonary TB in the current study 68(68%) is comparable to study conducted by Patil Shital et al 141(70.5%) patients with pulmonary tb with DM and 59(29.5%) had extra pulmonary TB.

TABLE 6: Comparision Of Incidence Of Extra-Pulmonary Tb With Other Authors:

In this study, amongst extra-pulmonary TB is pleural TB [31.2%] followed by TB lymphadenopathy [28.1%] was the commonest, which is comparable with studies done by **Anil Kumar Agarwala** et al and Patil Shital et al which had 11(31.4%) and 55(39%) of pleural TB.

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EXTRA-PULMONARY TB	OUR STUDY N(%)	ANIL KUMAR AGARWALA et al STUDY[24]n (%)	PATIL SHITAL ET AL STUDY[25]
ABDOMINAL TB	3(9.3%)	5(14.3%)	3(5.08%)
PLEURAL TB	10(31.25%)	11(31.4%)	55(39%)
CNS TB	3(9.3%)	4(11.4%)	2(3.38%)
BONE TB	3(9.3%)	3(8.6%)	-----
TB LYMPHADENOPATHY	9(28.12%)	4(11.4%)	29(49.15%)
DISSEMINATED TB	4(12.5%)	-----	-------

TABLE 7: Comparision Of X-Ray Findings With Other Studies:

In this study, amongst the patients with pulmonary Tb , majority had bilateral lower zone or multi zone involvement-27(39.7%) which is comparable to studies done by Auvthu S et al who had 27(57.5%) and another study by Shital P et al where the incidence was 41(29%). However the incidence of fibrocavitatory lesions were only 19.1% in the current study as compared to Auvthu S et al study which had 76% fibrocavitatory lesions.

	UPPER ZONE n(%)	U/L MID/LOWER ZONE n(%)	B/L LOWER ZONE OR MULTI-ZONE n (%)	FIBROCAVITATORY n (%)
Present Study	23(33.8%)	17(25%)	27(39.7%)	13(19.1%)
Auvthu S et al [26],	6(12.77%)	14(29.8%)	27(57.5%)	36(76%)
Shital P et al [25]	11(7.8%)	34(24.11%)	41(29%)	55(39%)

TABLE 8:Comparision Of Incidence Of Drug Resistant Tb With Other Study:

The incidence of MDR TB is slightly higher in the current study as compared to other study.

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	DRUG RESISTANT /MDR-TB	DRUG SENSITIVE
OUR STUDY	8.8%	91.2%
SHITAL P ET AL[25]	2.8%	98.2%

CONCLUSION:

In this study, the common manifestation of TB in diabetic patient was pulmonary TB [68%] with atypical chest x-ray findings i.e., lower zone or multi zone involvement which was associated with poor glycaemic control.Among group with poorly controlled diabetes [hba1c>10%], 67.9% people had bilateral lower zone opacities and 21.4% people had unilateral lower zone involvement, fibrocavitatory lesion was found only in this group [19.1%]. But only upper zone opacities were present in group with well controlled diabetes [hba1c<7.5%]

The most common extra-pulmonary manifestation seen among diabetic patients overall was pleural TB [31.25%], which was most frequently seen with well controlled and moderately controlled diabetes and was absent in poorly controlled diabetes. TB lymphadenopathy was the second common extra-pulmonary manifestation TB [28.1%]

Among group with poor glycaemic control [hba1c>10%],the most common extra-pulmonary manifestation of TB is disseminated TB and TB lymphadenopathy followed by bone TB.

Although the severity and manifestation of TB is effected by glycaemic status, the incidence of drug resistant TB is lesser among diabetic people which can be inferred from this study[19.1%]. But only upper zone opacities were present in group with well controlled diabetes [hba1c<7.5%]

The most common extra-pulmonary manifestation seen among diabetic patients overall was pleural TB [31.25%], which was most frequently seen with well controlled and moderately controlled diabetes and was absent in poorly controlled diabetes. TB lymphadenopathy was the second common extra-pulmonary manifestation TB [28.1%]

Among group with poor glycaemic control [hba1c>10%],the most common extra-pulmonary manifestation of TB is disseminated TB and TB lymphadenopathy followed by bone TB.

Although the severity and manifestation of TB is effected by glycaemic status, the incidence of drug resistant TB is lesser among diabetic people which can be inferred from this study.

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