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Co-Morbidity of Pulmonary Tuberculosis and Diabetes Mellitus- A Prospective Analysis

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ABSTRACT
Several studies have evaluated the relationship between diabetes mellitus (DM) and tuberculosis (TB), but the nature of this relationship is not fully understood. TB incidence may be influenced by immune suppression from DM, but this association may be confounded by other clinical and socioeconomic factors. We aimed to assess socio-demographic and clinical differences in TB patients with and without DM.A semi-Structured Proforma was used to collect the socio-demographic profile & clinical features, including the age, the sex, the site of the tuberculous pulmonary involvement seen on the chest roentgenogram of the patients. A fasting value >/= 129 mg/ dl & 2hrPPBS >/= 200 mg/ dl was considered as diabetes mellitus. Comparison of the clinical features was conducted after dividing them to 2 groups: - namely Group A (patients with sputum AFB positive tuberculosis and diabetes mellitus) & Group B (patients with sputum AFB positive tuberculosis without diabetes. Males were more affected than females. Most common age group affected was 51-60(52.05%). Out of 73 patients, 49 (67.1%) had the history of contact with tuberculosis. The presence of diabetes mellitus was found not to have a statistically significant effect on the patients' symptoms. DM and TB represent a critical intersection between communicable and non-communicable diseases in these countries and the effect of DM on TB incidence and outcomes provide numerous opportunities for collaboration and management of these complex diseases in the national public health programs.

Keywords: *Diabetes Melitus, Tuberculosis*

INTRODUCTION

Despite the Directly Observed Treatment Short course (DOTS) strategy, tuberculosis (TB) is still a major public health problem in the world [1.]Globally, there are an estimated 8.8 million new tuberculosis (TB) cases each year, and approximately 340 million people are living with diabetes[2,3.] Diabetes is a known risk factor for the development of active TB[4,5,6] and an estimated 15% of patients with TB in countries with a high TB burden have diabetes[7.]The association between diabetes and TB is an area of growing interest due to the persistently high prevalence of both diseases internationally and the expected increase in diabetes incidence and deaths over the coming decades[3,8,9] Diabetes is a debilitating disease that impairs the cellular immune system and provides the ground for TB. The WHO estimates that by 2030, the population of diabetics is increasing and reaches about 316 million people, most of them are living in developing countries [10,11.] According to the Center for Disease Control (CDC), the prevalence of DM in the United States is approximately 8% [12.] The leukocyte dysfunction and reduction of serum bactericidal activity in DM patients increases the risk of TB infection [13,14.] Patients with DM are at increased risk of pulmonary TB [15-22.]Tuberculosis in older people with weak immunity is associated with less cough and fever in compare with younger individuals while, pleural effusion and cavitation are more common in patients with normal immune responses [23.]

Although some epidemiological features of pulmonary tuberculosis such as gender, age and residential area are similar in both diabetic and non-diabetic patients, but in clinical point of view, radiological and laboratory features were more dominant in diabetic pulmonary tuberculosis-infected patients comparing with non-diabetics patients[24.]

AIMS

1. To find out the clinical pattern and the socio- demographic pattern of pulmonary tuberculosis among the patients with and without diabetes mellitus.
2. To find out the differences in the radiological presentation of pulmonary tuberculosis among patients with and without diabetes mellitus.

MATERIAL & METHODS

A hospital based, non interventional, prospective, study was conducted in the department of medicine, Pariyaram Medical College, Pariyaram, Kannur, Kerala, India. Study population was 73 consecutive adult patients of either sex. Inclusion Criteria were patients between 30 – 60 years of age of the either sex, known diabetic patients on treatment presenting with the respiratory symptoms who is sputum positive for the acid-fast bacilli, patients in whom sputum AFB positive pulmonary tuberculosis & diabetes mellitus were diagnosed simultaneously. Exclusion criteria were patients who fail to give the informed consent, patients below 30 years & above 60 years of age, patients who were HIV positive, patients with malignancy and patients on the immune suppressants. 73 patients satisfied the inclusion criteria. In each case, an informed consent was taken. A semi- Structured Proforma was used to collect the socio-demographic profile & clinical features, including the age, the sex, the site of the tuberculous pulmonary involvement seen on the chest roentgenogram of the patients.

Blood glucose was estimated with venous whole blood. A fasting value >/=129 mg/ dl & PPBS >/= 200 mg/ dl was considered as diabetes mellitus. Routine examination of the blood & Mantoux test were done. Comparison of the clinical features were conducted after dividing them to 2 groups: - namely Group A (patients with sputum AFB positive tuberculosis and diabetes mellitus) & Group B (patients with sputum AFB positive tuberculosis without diabetes). The tuberculin reaction and bacteriological findings of the two groups were compared. One early morning sputum samples and one spot sample were collected in a sterile container. AFB staining were

done from RNTCP designated microscopy centre. Postero-anterior view of the chest x ray were taken and reviewed by one pulmonologist .A cavitation was considered present only when its diameter was larger than 2 cm Radiological lesions were tabulated into zones and statistically analyzed. The radiographic findings of the two groups were compared.

Statistical Analysis

All the data collected were entered in & later analyzed using the Computer program, Statistical Packages for Social Sciences (SPSS) Version 7.5. Comparisons between the frequency variables were assessed through the chi-square test.

RESULT

A total of 73 patients were studied and the results were as follows.

Males were more affected than females with a male: female ratio of 5.63:1. Most common age group affected was 51-60(52.05%).The mean age of the presentation was 50.05 years for the study group. Standard deviation was 8.4. Majority of the patients belonged to the rural background. Out of 73 patients, 49 (67.1%) had history of contact with tuberculosis. This was not statistically significant with the comorbidity of diabetes. Group A included 38 patients of which half were newly detected with diabetes mellitus. The presence of diabetes mellitus was found not to have a statistically significant effect on the patients' symptoms.

Out of 73 patients, the majority, 35(47.9%) had 1+ TB bacillus in sputum sample, 27 (37%) had ++ & 11(15.1%) had +++ and no one had scanty positivity. This association was statistically significant with diabetes status. The majority of the patients of group A were smear-positive (2+) - 22 out of 38. The patients of group B were predominant in the 1+ category - 24 out of

Majority of the patients (66 i.e. 90.4%) were mantoux +ve. This was not statistically significant with diabetes status. Of these 37 patients had diabetes. Only 1 patient from group A was mantoux negative.

Radiological findings in tuberculosis and diabetes:31 (42.5%) out of 73 patients had left lower zone consolidation. Of these 29 had diabetes. 14(19.2%) out of 73 patients had right upper zone fibrosis. Of these majority were non-diabetic. 10(13.7%) out of 73 patients had right upper zone consolidation. Of these majority were not diabetic. Only two of the 73 (2.7%) had cavitary disease confined to the lower lung fields.Group A patients had increased frequency of lung lesions confined to the lower lung zone compared to group B (29% versus 2%). Group A patients had significantly higher frequency of lung consolidation lesions compared to Group B (29% versus 2%). Consolidation was more frequently confined to lower lung zone in patients with diabetes(28.9% versus 2.5%).

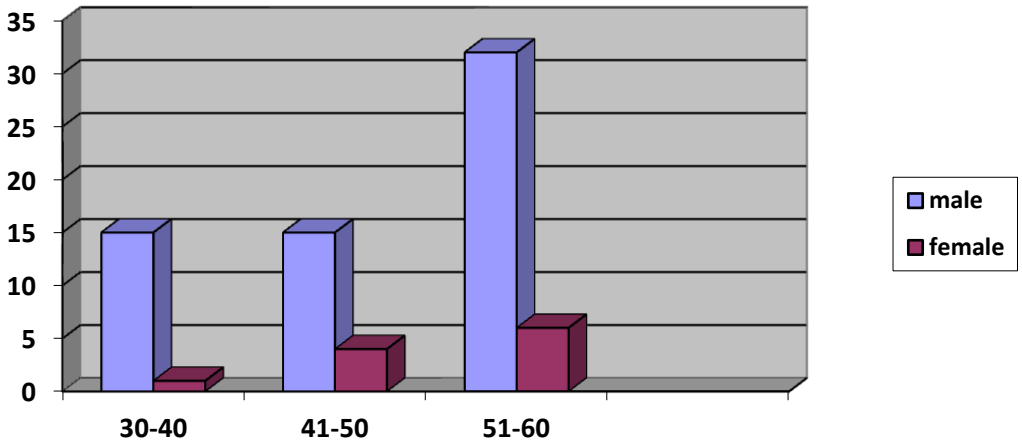

Figure1 Graphical Representation Of The Age-Sex Distribution:

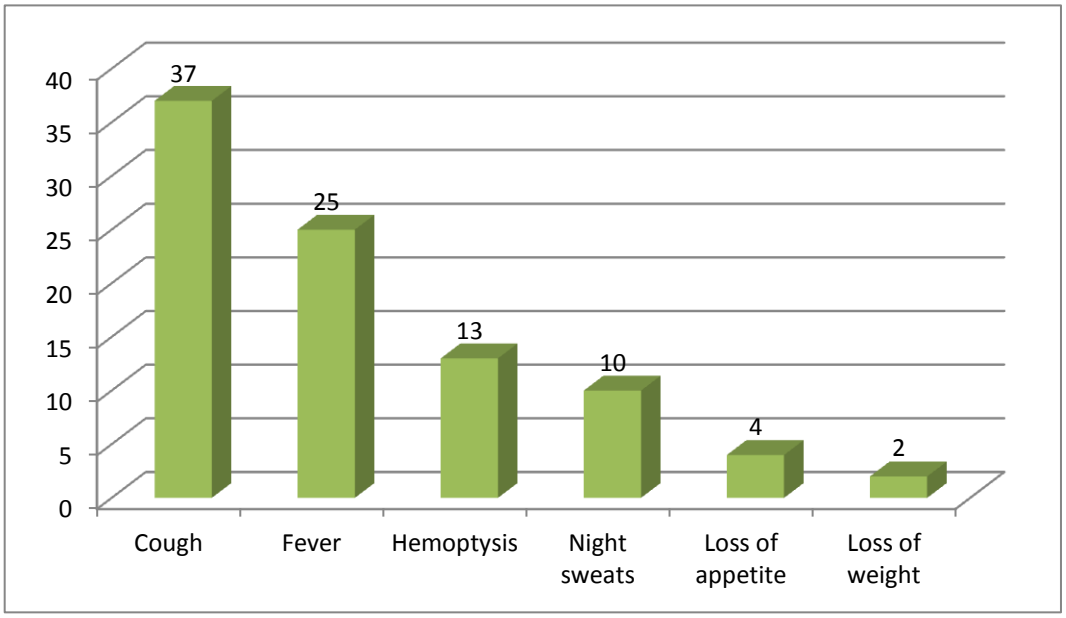

Figure2 Symptoms:

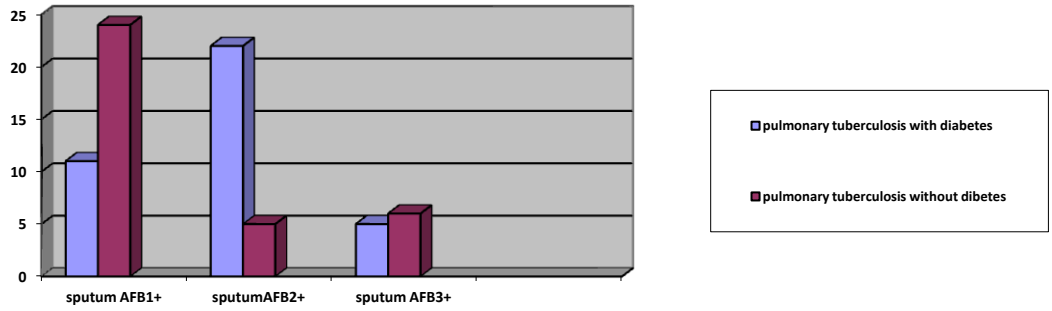

Figure 3 Sputum Positivity And Diabetes

Table-1 Comparison Of Radiological Presentation In Diabetic And Non-Diabetic Patients
RUL CON- Right upper lobe consolidation. RULF-Right upper lobe fibrosis. RULCAV-Right upperlobecavitation
RULCOL Right upperlobe collapse. RML-Right middle lobe. RLL-Right lowerlobe

Site		Diabetic		Non-diabetic		p value
		No.	%	No.	%	
RULCON		2	5.3	8	22.9	0.04 *(F)
RULF		2	5.3	12	34.3	0.002 *
RULCAV		4	10.5	3	8.6	0.999 (F)
RULCOL		0	0	1	2.9	0.479 (F)
RMLCON		5	13.2	4	11.4	0.999 (F)
RMLF		0	0	1	2.9	0.479 (F)
RMLCAV		0	0	0	0	-
RMLCOL		0	0	1	2.9	0.479 (F)
RLLCON		2	5.3	1	2.9	0.999 (F)
RLLF		0	0	0	0	-
RLLCAV		0	0	0	0	-
RLLCOL		0	0	0	0	-
LULCON		4	10.5	4	11.4	0.999 (F)
LULF		0	0	0	0	-
LULCAV		8	21.1	3	8.6	0.136
LULCOL		1	2.6	0	0	0.999 (F)
LLLCON		28	73.7	3	8.6	< 0.001*
LLLF		0	0	0	0	-
LLLCAV		1	2.6	0	0	0.999 (F)
LLLCOL		0	0	0	0	-
EFFN	RIGHT	1	2.6	1	2.9	0.388
	LEFT	2	5.3	0	0	

F – Fisher's exact test (used when more than 20% of cells have expected frequencies less than 5)

Rest all using Chi-square test.

DISCUSSION

Patients with diabetes mellitus as a group are more susceptible to a more aggressive course of tuberculosis[25]. Population ageing, urbanization and associated lifestyle changes have propelled the rapid increase in rates of non-communicable diseases (NCD) and among these is diabetes mellitus (DM)[26]. DM, in particular, type 2 DM, is a global epidemic that emerged over last three decades as a consequence of the epidemic of obesity [27,26]. DM depresses the immunologic response that facilitates the development of infectious diseases, including infection by Mycobacterium tuberculosis, the agent of TB [28]. The health burden associated with these disorders is high and may increase further as the incidence of DM increases [29,30]. According to the World Health Organization about 10% of TB cases globally are linked to diabetes [31].In countries with similar burden of TB, such as Mexico [32], India [33], and anzania [34], the prevalence of DM among TB patients was 2.7%, 18.4%, and 6.7% respectively. On the other hand, in low-burden countries, such as Canada [35] and Finland [36]the prevalence was 0.14% and 14.6% respectively. The majority of the sample were males-62 (84.9%). This is in agreement with previous studies[37,46,47].This feature has been

mostly attributed to the socio-cultural factors that lead to a higher risk of exposure to Mycobacterium tuberculosis in men and / or a higher frequency of the under diagnosis in the women, mainly due to the lower level of access to the medical services. Distinct differences in the epidemiology of tuberculosis are observed between developing and industrialized nations by Raviglione et al (1995)[38] From this study, it would appear that tuberculosis attacks the patients with diabetes in the latter half of life. (Similar to studies of Ezung et al-2002[39]). No statistically significant association has been found with the age and the diabetes. The most frequent symptom was cough. Loss of weight was rare. The presence of diabetes mellitus was found not to have a statistically significant effect on patients' symptoms. (similar to studies of Feza Bacakoglu, 2001[40] .The majority of the diabetic patients were sputum positive (2+) 22 out of 38. This may indicate that in patients with diabetes, tuberculosis has the relative paucity of the physical signs and the diagnosis is made at the far advanced stages. In other words, the chances of isolating the tuberculosis bacillus in the sputum of diabetic TB patients are more than non-diabetic patients.

These findings are in agreement with other studies in this subject [25,41,] because these patients are associated with increased sputum production, and also because of more cavitation and tissue immune inhibition, the possibility of access to further sputum containing bacilli exist. The presence of diabetes mellitus was found to have a statistically significant effect on the localization of the pulmonary infiltrates. In diabetic patients, left lower lobe consolidation was predominant (72.5%); while in non diabetic patients, 2(6.1%) had this. Lower lung field tuberculosis was significantly associated with diabetics. (similar to the studies of Feza Bacakoglu, 2001[40],Shaikh et al, 2003)[42]

Our studysupport the original observation of Sosman and Steidl[43] that tuberculosis tends to occur predominantly in the lower lung zone in the patients with diabetes. Another study by Weaver[44] also shows unusual lower lung zone in 20 cases with co-existing pulmonary tuberculosis and diabetes mellitus. A similar study conducted by P. Ravindran at Trivandrum medical college, Kerala shows 13.81% (9 out of 65) of lower zone tuberculosis in diabetic patients[45].

CONCLUSION

Tuberculosis and diabetes frequently coexist with predominant incidence in the adult males. The presence of diabetes mellitus may not alter the symptoms of pulmonary tuberculosis. prevalence of non communicable disease continues to rise in developing countries, especially with the rise of elderly population, the prevention and treatment of infectious diseases will be urgent. DM and TB represent a critical intersection between communicable and non-communicable diseases in these countries and the effect of DM on TB incidence and outcomes provide numerous opportunities for collaboration and management of these complex diseases in the national public health programs.

Limitation: Small size of population studied. Single centered study

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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