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A COMPARATIVE STUDY – CLINICORADIOGRAPHICAL PROFILE OF PULMONARY TUBERCULOSIS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS & NON DIABETIC PATIENTS

Medicine

Dr. Sonika Chaudhary 3rd Year P.G Resident Department Of Medicine Geetanjali Medical College, Udaipur, Rajasthan

Dr. Y. N Verma* Professor Department Of Medicine Geetanjali Medical College, Udaipur, Rajasthan
*Corresponding Author

ABSTRACT

Tuberculosis is a communicable disease that is a major cause of ill health, and one of the top 10 causes of death worldwide and the leading cause of death from a single infectious agent (ranking above HIV/AIDS). CBNAAT marks an important development in the field of rapid molecular tuberculosis diagnosis. Diabetes triples the risk of developing tuberculosis, and poor glycemic control adversely affects tuberculosis treatment outcomes with effects such as prolongation of culture conversion, treatment failure, relapse, and death.

KEYWORDS

Clinicoradiographical, Pulmonary, Tuberculosis

INTRODUCTION:

Tuberculosis is a communicable disease that is a major cause of ill health, and one of the top 10 causes of death worldwide and the leading cause of death from a single infectious agent (ranking above HIV/AIDS). It is caused by the bacillus Mycobacterium tuberculosis, which is spread when people who are infected with Tuberculosis expel bacteria into the air; for example, by coughing, sneezing and speaking. Tuberculosis had been a perennial associate of human life and history of tuberculosis is almost coexisting with the history human civilization.

The large scale implementation of the Indian government's Revised National TB Control Program (RNTCP) (sometimes known as RNTCP I) was started in 1997. This program was then expanded across India until the entire nation was covered by the RNTCP in March 2006. At this time the RNTCP also became known as RNTCP II. RNTCP II was designed to consolidate the gains achieved in RNTCP I, and to initiate services to address TB/HIV, MDR-TB and to extend RNTCP to the private sector.

The initial objectives of the RNTCP in India were:

- to achieve and maintain a tubercular treatment success rate of at least 85% among new sputum positive (NSP) patients.
- to achieve and maintain detection of at least 70% of the estimated new sputum positive people in the community.

New sputum positive patients are those people who have never received tuberculosis treatment before, or who have taken tubercular drugs for less than a month. They have also had a positive result to a sputum test, which diagnoses them as having tuberculosis.

As per the recent RNTCP guidelines, presumptive Pulmonary Tuberculosis refers to a patient with any of the symptoms or signs of Tuberculosis :

- Cough> 2 weeks,
- Fever > 2 weeks,
- Significant weight loss,
- Haemoptysis,
- any abnormalities in the chest radiograph.

Early case detection is vital to interrupt the transmission and treatment of tuberculosis. Direct sputum smear microscopy is the cornerstone for the diagnosis of tuberculosis in resource-limited settings, but it has only modest (35-80%) sensitivity and a poor Positive Predictive Value (PPV). Culture is the “gold standard” for final determination and also permits drug susceptibility testing. However, it remains largely inaccessible in resource limited settings as a result of infrastructure and financial limitations. Even where accessible, culture results are typically not available for 2-6 weeks.

RNTCP screens around 20 million TB symptomatic by microscopy and initiates around 1.5 million cases of TB on treatment annually since 2007-08. Rapid molecular diagnostics introduced since 2009 and scaled up from 2012 onwards has ensured that line probe assay and cartridge based nucleic acid amplification test (CBNAAT) testing is available throughout the country. In 2016, 5,20,000 patients have been tested and 35,000 rifampicin resistant/MDR-TB patients have been diagnosed.[1]

CBNAAT marks an important development in the field of rapid molecular tuberculosis diagnosis. This assay was rapidly endorsed by the World Health Organization in December 2010 as a replacement for sputum smear microscopy, particularly in settings with high rates of HIV-associated TB and multidrug-resistant TB developed for testing sputum samples.

CBNAAT test is a semi-quantitative nested real-time PCR in-vitro diagnostic test with two uses-

a. The detection of Mycobacterium tuberculosis complex DNA in sputum samples or concentrated sediments prepared from induced or expectorated sputum that are either Acid-Fast Bacilli (AFB) smear positive or negative.
b. The detection of rifampicin resistance associated mutations of the rpoB gene in samples from patients of rifampicin resistance.

Imaging has an important role in the initial evaluation of patients suspected of having active tuberculosis. Primary tuberculosis demonstrates radiographical findings that include lymphadenopathy, consolidation, pleural effusion, and miliary nodules. Post primary tuberculosis demonstrates consolidations that are predominant in the apical and upper lung zones, nodules, and cavitation.

So radiology is important in the management of tuberculosis for :

1- Active and passive case finding.
2- Confirmation of diagnosis in symptomatic patients.
3- Showing the extent and pattern of the disease.
4- Prediction and assessment of complications.
5- Monitoring response to therapy (whether medical or surgical)

Diabetes triples the risk of developing tuberculosis, and poor glycemic control adversely affects tuberculosis treatment outcomes with effects such as prolongation of culture conversion, treatment failure, relapse, and death.

Furthermore, diabetes accounted for 10·6% of global tuberculosis deaths among HIV-negative individuals in 2015.With 425 million people affected by diabetes globally in 2017, and a predicted 48% increase up to 629 million people who would have diabetes in 2045, it is foreseeable that this surge in the prevalence of diabetes will contri bute to increase the incidence of tuberculosis.

Unfortunately, the regions with the current highest burden of tuberculosis would also experience the biggest increase in diabetes prevalence[4]

Diabetes Mellitus refers to a group of common metabolic disorders that share the phenotype of hyperglycaemia. The prevalence of type 2 Diabetes Mellitus is rising much more rapidly, presumably because of

increasing obesity, reduced activity levels, as countries become more industrialized and the aging of the population.

WHO criteria for the diagnosis of Diabetes Mellitus :
- Symptoms of diabetes plus random blood sugar> 200mg/dl
- Fasting blood sugar> 126mg/dl
- HbA1c≥ 6.5%
- 2h post-prandial blood sugar≥ 200mg/dl

AIM AND OBJECTIVES
1. To study the Clinical and radiographical profile of Pulmonary Tuberculosis in patients with type 2 Diabetes Mellitus & Non Diabetic Patients
2. Comparison of Clinicoradiographical profile of pulmonary tuberculosis in diabetic and non-diabetic patients regarding the age of presentation, symptomatology, haematological profile, sputum positivity and chest radiographical findings.

MATERIAL AND METHODS
SOURCE OF DATA;
This study was conducted in Geetanjali Medical College And Hospital, Udaipur, Rajasthan. Two groups each of 49 patients were studied. To each patient the nature and purpose of study was explained and his/her oral consent was taken.

SAMPLE SIZE:
$n = 2(Z\alpha + Z\beta)^2 P(1 - P)/ E^2 = 98$

Here Zα is 95% confidence level = 1.96 Zβ 80% power of study = 0.8143 E is allowable error of 20% and P is proportion of diabetic and non-diabetic to be 0.50 which is unbiased situation.

Patients were selected from the different units of Department of Medicine. The first group comprised of 49 known or newly diagnosed cases of Diabetes suffering concomitantly with pulmonary tuberculosis. Detailed history pertaining to diabetes and pulmonary tuberculosis was taken like symptoms and duration of those symptoms. After completing history, patients were carefully examined in detail.

Patients past records were carefully reviewed to ascertain his past glycemic status and treatment. The patient was then investigated by the following:
1. Complete blood count
2. Erythrocyte sedimentation rate- it was done in citrated sample of blood drawn by Westergren method
3. Sputum microscopic examination for acid fast bacilli by Zeihl Neelsen's method
4. Fasting blood glucose, random blood glucose and HbA1C levels.
5. Chest radiograph PA view- it was taken before initiating antitubercular therapy
6. Cartridge Based Nucleic Acid Amplification test (CBNAAT)

In the second group 49 non-diabetic patients suffering from pulmonary tuberculosis were taken. These patients were selected without prior knowledge of their bacteriological status and radiological picture. Diabetes was excluded in this group by estimation of fasting and random blood sugar levels in every patient. In this group also detailed history pertaining to tuberculosis was taken and examination was done alongwith above mentioned investigations.

INCLUSION CRITERIA:
- Patient aged more than 18 year of age
- Patients with type 2 diabetes mellitus diagnosed as per WHO criteria
- Patients with cough > 2 weeks; fever > 2 weeks; significant weight loss; haemoptysis; any abnormalities in chest radiography .

EXCLUSION CRITERIA:
- Patient suffering from HIV
- Patient who is suffering from other immuno compromised states like malignancy, chemotherapy, patients on steroid therapy.

Above inclusion and exclusion criteria will be confirmed with history and investigations

RESULTS
Table1: Symptomology of Tuberculosis In The Diabetic And Non-Diabetic Patients

Symptoms	Diabetic		Non-Diabetic		P-value
	No. of Patients	Percent	No. of Patients	Percent	
Cough	49	100	49	100	-
Sputum	49	100	49	100	-
Haemoptysis	14	28.57	25	51.02	0.019
Fever	34	69.38	24	48.97	0.580
Weight Loss	22	44.89	10	20.40	0.009

Among the diabetic patients, all 49 patients had cough and sputum, 14 patients had haemoptysis, 34 had fever and 22 patients had weight loss. Among the non-diabetic patients, all 49 had cough and sputum, 25 patients had haemoptysis, 24 patients had fever and 10 patients had weight loss.

Figure1: Symptomology of Tuberculosis In The Diabetic And Non-Diabetic Patients

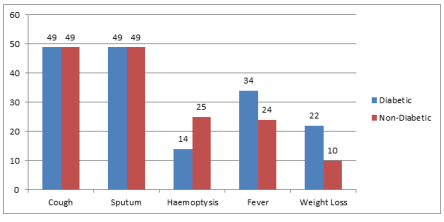


Table2: Positivity Of Sputum For AFB (ZN Staining) Of Tuberculosis Patients In The Diabetic And Non-Diabetic Patients

	Diabetic		Non-Diabetic		P-value
	No. of Patients	Percent	No. of Patients	Percent	
Sputum Positive for AFB	36	73.46	27	55.10	<0.05

Among the diabetic patients 36 patients had Sputum Positive for AFB. On the other hand, in the non-diabetic patients, 27 patients were found to be Sputum Positive for AFB.

Figure2: Positivity Of Sputum For AFB (ZN Staining) Of Tuberculosis Patients In The Diabetic And Non-Diabetic Patients

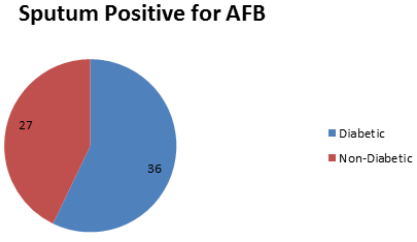
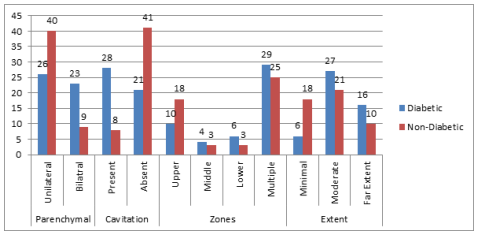


Table3: Distribution of Various Radiographical Presentation of Tuberculosis in Diabetic and Non-Diabetic Patients:

Radiolograhical Feature	Diabetic		Non-Diabetic		P-value
	No. of Patients	Percent	No. of Patients	Percent	
Parenchymal					
Unilateral	26	53.06	40	81.63	.002
Bilateral	23	46.93	9	18.36	
Cavitation					
Present	28	57.14	8	16.32	0.000
Absent	21	42.85	41	83.67	
Zones					
Upper	10	20.40	18	36.73	0.293
Middle	4	8.16	3	6.12	
Lower	6	12.24	3	6.12	
Multiple	29	59.18	25	51.02	
Extent					
Minimal	6	12.24	18	36.73	0.017
Moderate	27	55.10	21	42.85	
Far Advanced	16	32.65	10	20.40	

Among the 49 diabetic patients, 26 patients had unilateral Parenchymal involvement while in non-diabetic patients 40 patients had unilateral involvement. Out of 49 diabetic patients 28 patients had cavitation while among non diabetic patients only 8 patiets had cavitation. 29 diabetic patients with tuberculosis were found to have multiple zone involvement while in non diabetic patients group 25 patients had similar observations. Extent of tuberculosis was moderate in 27 and 21 patients in diabetic and non diabetic group wth tuberculosis respectively.

Figure 3: Distribution of Various Radiographical Presentation of Tuberculosis in Diabetic and Non-Diabetic Patient



DISCUSSION

The current study was carried out to study the clinicoradiographical profile of pulmonary tuberculosis in patients with type 2 Diabetes Mellitus and non-diabetic patients.

In the current study Among the 49 diabetic patients, 26 patients had unilateral Parenchymal, 28 of the patients had Cavitation which was similar to Hendy and Stableforth (1983)[70], tuberculosis was situated in multiple zones for 29 patients and the extent of tuberculosis was moderate in 27 patients. Among the 49 non-diabetic patients, 40 patients had unilateral Parenchymal, 8 of the patients had Cavitation, tuberculosis was situated in multiple zones for 25 patients and the extent of tuberculosis was moderate in 21 patients. In the present study, upper zone lesion was seen in 10 diabetic patients and 18 non-diabetic patients, which is similar to the findings of Gupta et al. (1996)[76] who found upper zone involvement in 22.2% diabetic patients and 30.2% in non-diabetic. Further, like the findings of Gupta et al. (1996), the present study also found limited patients in middle zone and lower zone in both diabetic and non-diabetic groups and maximum patients were in multiple zone.

As per the study of Dousa et al., (2019) 43 diabetic patients had bilateral Parenchymal and 35 non-diabetic patients had bilateral Parenchymal. For majority in the diabetic and non-diabetic group of the patients tuberculosis was located in the upper lobe. Cavitation was present in majority of the diabetic and non-diabetic patients. Thus, caviation was present in more number of diabetic patients as compared to non-diabetic, which is similar to the study by Deshmukh and Shaw (1984)[71], Kishore et al. (1973)[91] and Holden and Hiltz (1962)[62].

Further, the findings of present study related to extent of tuberculosis was also similar to Deshmukh and Shaw (1984), Gupta et al. (1996) and Holden and Hiltz (1962) who also found limited patients with minimal and far advanced lesion in both diabetic and non-diabetic groups and maximum patients with moderately advanced tuberculosis lesions.

All of AFB negative samples came to be positive with CBNAAT indicating CBNAAT assay is highly sensitive and specific technique. The result of the study revealed a maximum positivity rate by CBNAAT, which indicated that it is a more sensitive technique as compared to conventional methods.

Rifampicin resistance was detected only in two diabetic patients and one non diabetic patient so this implies that prevalence of Multi-drug resistant tuberculosis was not found to be significant in both the groups.

SUMMARY

- All diabetic patients had cough and sputum, while 14 had haemoptysis, 34 had and 22 had weight loss. On the other hand, all non-diabetic had cough and sputum, 25 had haemoptysis, 24 had fever and 10 had weight loss.
- 36 diabetic patients had Sputum Positive for AFB, while only 27 non-diabetic patients were found to be Sputum Positive for AFB
- Out of 49 diabetic patients, 26 had unilateral Parenchymal, 28 had Cavitation, 29 had multiple zone tuberculosis and the extent of tuberculosis was moderate in 27 patients. On the other hand, out of 49 non-diabetic patients, 40 had unilateral Parenchymal, 8 Cavitation, 25 had multiple zone tuberculosis and the extent of tuberculosis was moderate in 21 patients.
- Majority of the diabetic patients (n = 22) had Hb 8.1-10 gm%, similarly majority of the non-diabetic patients (n = 18) had Hb 8.1-10 gm%.
- Majority of the diabetic patients (n = 41) had TLC 4-11000 cells/mm3, similarly, majority of the non-diabetic patients (n = 35) had TLC 4-11000 cells/mm^3.
- Majority of diabetic patients (n = 23) had ESR between 51-100 mm, similarly, , majority of the non-diabetic patients (n = 25) had ESR between 51-100 mm.
- According to the scanty sputum grading, majority of the patients showed moderate advanced on the X-ray.
- Out of 49 diabetic patients, majority of the patients (n = 28) had FBS from151-200.
- Out of 49 diabetic patients, majority of the patients (n = 43) had RBS from 201-300.

CONCLUSION

The study showed a male predominance. The present study shows that chest radiography is simple and cost effective method for identification of pathological findings in pulmonary tuberculosis patients. Hemoptysis is more frequent in non diabetic patients while weight loss is common finding in diabetic patients with pulmonary tuberculosis. Sputum positivity rate is higher in diabetics. CBNAAT was found to be positive all sputum negative patients thus it is a very highly sensitive tool for the diagnosis of pulmonary tuberculosis. Bilareral and far advanced tuberculosis with cavitation are common in diabetics. The signs and symptoms were found to be more rigorous in the diabetic patients with TB. The Diabetic group is more likely to present with atypical radiological images. Thus diabetes predisposes to clinically and radiologically severe and advanced tubercular disease. Among diabetic patients presenting with lower lung field lesions or cavities, possibility of tuberculosis should always be considered for prompt diagnosis and management.

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