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RESEARCH ARTICLE

CLINICAL AND RADIOLOGICAL STUDY OF PULMONARY TUBERCULOSIS IN DIABETES MELLITUS

Dr. Abhishek Nigam¹ and Dr. Prakash Joshi²

1. Postgraduate Student, Dept. of Gen. Medicine, Sri Aurobindo Medical College & PG Institute-Indore.
2. Professor Dept. of Gen. Medicine, Sri Aurobindo Medical College & PG Institute-Indore.

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Abstract

Background: Tuberculosis is the third most important communicable disease in Egypt follows the schistosomiasis. The association between TB and DM has been known for thousands of years, Although the incidence of TB is declining slowly, the burden of diabetes is increasing very rapidly, many studies have been performed to answer about the effect of type 2 DM in clinical, radiological and the outcome of pulmonary tuberculosis, however there is still a huge gap of knowledge about the synergetic effect of the two diseases. The objective was to study the clinical and radiological profile of pulmonary tuberculosis among patients having diabetes mellitus (DM). **Methods:** The study was conducted at the department of general medicine, in a SAIMS Hospital. The study included pulmonary tuberculosis (PTB) patients with diabetes mellitus and the patients who were smear positive for pulmonary tuberculosis (control group) who met the criteria to participate in the study after a thorough examination. Informed written consent was obtained from all patients before enrolment.

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Introduction:-

Tuberculosis (TB) is an infectious disease caused by the bacterium *Mycobacterium tuberculosis*. It is an airborne disease, spread from person to person through the coughing, sneezing, speaking or singing of a person with active pulmonary TB disease. Some of the risk factors for developing TB disease include malnutrition, alcoholism, immunosuppressant (due to either disease Diabetes, CKD etc.. or medication), and the postpartum period. Despite being a preventable and curable disease, TB kills nearly two million people every year, mostly in developing countries.¹

A new study released shows that diabetes increases the risk of tuberculosis (TB) threefold, and the finding makes it important that India, which has the world's highest population of people affected with both the conditions, carries out a systematic assessment of the association. Diabetes Mellitus increases the risk of active Tuberculosis; say diabetes could be contributing as much as 10% of TB cases in India and China.

Several studies have highlighted Diabetes as a risk factor for tuberculosis. Diabetes is risk factor for developing active TB. There is strong evidence for this association with studies examining the incidence of TB showing it to be 2 to 5 times higher in diabetic patient than non-diabetic patients. Calculations from epidemiological model in India

Corresponding Author:- Dr. Abhishek Nigam

Address:- Postgraduate Student, Dept. of Gen. Medicine, Sri Aurobindo Medical College & PG Institute-Indore.

suggest that DM accounts for 14.8% of pulmonary TB and 20.2% smear- positive TB. DM has been found to be independently associated with an unfavorable outcome of pulmonary TB. TB in diabetic patient has been reported to have cavitary lesions, less sputum positivity and paucity of symptoms and sign compared to TB in non-diabetic patients. DM has been found to be risk factor for deaths in TB patient. The only way to counter this dreadful combination is to insist on routine blood sugar screening test in TB patient and carry out sputum and X-ray examination in diabetes once a year or on any occasion when patient gets cough of any duration or insulin requirement suddenly goes up.¹

Clinicians say's they have long observed the association between the two diseases, but haven't effectively determined whether diabetes causes TB, or vice versa. We have known this for long, but due to limited resources, India has focused on fighting multi drug resistant TB and other infectious diseases, and not cared to maintain a registry to track the correlation of the two diseases. This cannot be ignored for a long time. The new findings are also consistent with emerging scientific data on the biological mechanisms by which a diabetic condition called hyperglycemia (high blood sugar) may affect a person's immune response (defense against an infection) to TB. Researchers admit limitations to the study, which among other things, has not studied how age and type of diabetes affects the causal relationship. So, they recommend further studies investigating how TB varies by type, duration and severity of diabetes. Experts, however, say the new finding is still an eye opener as India battles merging epidemics of diabetes and TB. The study showed difference in weight between the DM/TB group and DM group which may explained with the effect of TB in the BMI by its microbial activity and by increase hyperglycemic state; this coincide with study on association between body mass index and diabetes mellitus in tuberculosis patients in China².

Aim

To study the difference in manifestation between well controlled and uncontrolled DM.

Background

Tuberculosis is a bacterial disease spread from one person to another principally by airborne transmission. The causal agent is *Mycobacterium tuberculosis* (the tubercle bacillus). In a small proportion of cases, the bacillus is transmitted to humans from infected cows through drinking non-sterilized milk. This mode of transmission plays only a minor role in the natural history of the disease in humans. Tuberculosis can affect any organ in the body. Pulmonary tuberculosis is the most frequent site of involvement; extra pulmonary tuberculosis is less frequent. Only pulmonary tuberculosis is infectious. About one-quarter of the world's population has latent TB, which means people have been infected by TB bacteria but are not (yet) ill with the disease and cannot transmit the disease. Tuberculosis (TB) is one of the top 10 causes of death worldwide. In 2016, 10.4 million people fell ill with TB, and

1.7 million died from the disease (including 0.4 million among people with HIV). Over 95% of TB deaths occur in low- and middle-income countries. Seven countries account for 64% of the total, with India leading the count, followed by Indonesia, China, Philippines, Pakistan, Nigeria, and South Africa. In 2016, an estimated 1 million children became ill with TB and 250 000 children died of TB (including children with HIV associated TB). TB is a leading killer of HIV-positive people: in 2016, 40% of HIV deaths were due to TB. Multidrug-resistant TB (MDR-TB) remains a public health crisis and a health security threat. WHO estimates that there were 600000 new cases with resistance to rifampicin the most effective first-line drug, of which 490 000, In 2012, it was estimated that 2.3 million TB cases occurred in India out of 8.6 million incidence of TB cases that were recorded globally.⁶ Diabetes prevalence was found to be 7.1% in India in the adult population.⁶

Global impact of TB1

TB occurs in every part of the world. In 2016, the largest number of new TB cases occurred in Asia, with 45% of new cases, followed by Africa, with 25% of new cases.

In 2016, 87% of new TB cases occurred in the 30 high TB burden countries. Seven countries accounted for 64% of the new TB cases: India, Indonesia, China, Philippines, Pakistan, Nigeria, and South Africa. Global progress depends on advances in TB prevention and care in these countries.

Symptoms and diagnosis

Common symptoms of active lung TB are cough with sputum and blood at times, chest pains, weakness, weight loss, fever and night sweats. Many countries still rely on a long-used method called sputum smear microscopy to

diagnose TB. Trained laboratory technicians look at sputum samples under a microscope to see if TB bacteria are present. Microscopy detects only half the number of TB cases and cannot detect drug-resistance. The use of the rapid test Xpert MTB/RIF (CBNAAT-Cartaige based nucleic acid amplification test) has expanded substantially since 2010, when WHO first recommended its use.

Treatment

TB is a treatable and curable disease. Active, drug-susceptible TB disease is treated with a standard 6 month course of 4 antimicrobial drugs that are provided with information, supervision and support to the patient by a health worker or trained volunteer. Without such support, treatment adherence can be difficult and the disease can spread. The vast majority of TB cases can be cured when medicines are provided and taken properly. Between 2000 and 2016, an estimated 53 million lives were saved through TB diagnosis and treatment. Recently, RNTCP has launched daily regimen for tuberculosis.¹

Diabetes Overview³

Diabetes is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces. Insulin is a hormone that regulates blood sugar. Hyperglycemia, or raised blood sugar, is a common effect of uncontrolled diabetes and over time leads to serious damage to many of the body's systems, especially the nerves and blood vessels. In 2014, 8.5% of adults aged 18 years and older had diabetes.

Material and Methods:-

The present study was conducted in a tertiary care hospital from June 2017 to November 2020.

Source of data:

Patients admitted in medicine ward of tertiary care hospital.

Sample size:

Total 50 patients were included in the study.

Inclusion criteria:

Patients admitted in Medicine ward, Medicine OPD.

Exclusion criteria:

1. Patients who did not give consent for study.
2. Diabetic patients with extra-pulmonary TB.
3. Patients of Pulmonary TB not having DM.

Data collection:

We confirmed that the patient had Diabetes Mellitus based on symptomatology and investigations. Confirmation of Tuberculosis was based on signs and symptoms, sputum for AFB, Chest X-ray.

We also included the patient previously diagnosed cases of diabetes mellitus.

Patients with pulmonary TB with Diabetes Mellitus were studied for signs and symptoms, chest X-ray findings and sputum for AFB.

Differences in clinical and radiological presentations of controlled and uncontrolled diabetes mellitus were studied.

Investigations and Monitoring. All patients were subjected to the following investigations: Haemoglobin, Whole Blood count, Urine examination, Kidney function test, Liver function test, Thyroid function test when needed, Sputum AFB, Chest x-ray, Blood glucose levels- fasting ,postmeal. Urine Examination – Sugar,Protein . HbA1c. (AUTOPURE HBA1c reagent used .According to National Glycohemoglobin Standerdisation Programme.)

Result:-**Table 1:-** Age wise Distribution.

Sr. No.	Age Group (years)	Frequency	Percent
1	13-30	5	10.0%
2	31-45	18	36.0%
3	46-60	21	42.0%
4	61-70	6	12.0%
	Total	50	100.0%
	Mean \pm SD	47.12 \pm 12.172	
	Range	19-75	

Number of patients were from age group 46-60 yrs i.e.21 in number (42%) followed by 31-45 yrs 18 (36%), and 61-70 (12%).Distribution of age group is as per Dr Chaya B E101 et al In the serial number 1, age group 13 to 30 years ,13 is taken because less than 12 years is considered in pediatrics.

Table 2:- Smoking.

Sr. No.	Smoking	Male (%)	Female (%)
1	Present	26 (70.02)	01 (7.69)
2	Absent	11(29.72)	12 (92.30)
	Total	37 (100)	13 (100)

The above table shows that 70% of males had history of smoking. One tribal female also happened to be a smoker.

Table 3:- Duration of DM.

Sr. No.	Duration	Frequency	Percent (%)
1	< 1	22	44.0%
2	2-5	17	34.0%
3	6-10	6	12.0%
4	> 10	5	10.0%
	Total	50	100.0%
	Mean	3.60	4.204
	Range	0.1-15yrs	

Out of 50 patients maximum number of patients were DM since < 1 yr i.e. 22 in number (44%) followed by 2-5yrs (34%).(Distribution of DM duration as per Dr Chaya B E et al.)

Table 4:- X ray: Type of Lesions.

Sr. No.	Type of lesion	Frequency	Percentage
1	Cavitatory Lesions	18	36%
2	Infiltrates	11	30%
	Non homogenous		
4	Miliary shadows	06	12%
	Pleural Effusion with olidation		
	Total	50	100%

X-ray findings (type of lesion) of the patients- Cavitatory lesion was in maximum number (36%) followed by infiltration (30%), non-homogenous opacities, miliary shadows (12%). There were 5 (10%) patients of pleural effusion with consolidation. Since pleural effusion alone is extra pulmonary TB, we have not included such cases.

Table 5:- Fasting Blood sugar.

Sr. No.	Fasting Blood sugar	Frequency	Percent	P value
1	< 126	11	22.0%	0.07
2	126-150	9	18.0%	
3	151-200	21	42.0%	
4	210-300	7	14.0%	
5	> 300	2	4.0%	
	Total	50	100.0%	
	Mean	166.64±58.294		
	Range	65-318		

Maximum number of patient was having fasting blood sugar in between 151-200mg/ml i.e. 21 in number (42%) followed by < 126 mg/ml (22%), 126-150 (18%), 210-300 (14%). There were only 2 patients having fasting blood sugar more than 300mg/ml. This difference of TB infection in relation to different levels of fasting blood sugar was not statistically significant. (p value > 0.05). (Distribution of fasting blood sugar . group is as per Dr Chaya B E et al.)

Out of 50 patients, 7(14%) were diagnosed Diabetes in Tuberculosis and 43(86%) were diagnosed Tuberculosis in Diabetes.

The maximum number of patients were on oral hypoglycaemic agents i.e. 23 in number (46%) followed by insulin (38%). 16% patients were on both oral hypoglycaemic agents and insulin for diabetes mellitus. This difference was not statistically significant. (p value > 0.05).

There were co-morbidities present like CVA with IHD (4%), Uraemia with DM Nephropathy (6%), Hydropneumothorax (4%), DM with DKA(4%).

Discussion:-

The increasing prevalence of diabetes mellitus with pulmonary tuberculosis is an important global issue associated with poverty, inadequate education, malnutrition, urbanization, and crowded living condition .This study has been conducted in tertiary care hospital. In the present study, the number of patients below the age of 50 were 74% and peak incidence was in the age groups of 46-60yrs and 31- 45yrs.

44% patients had duration of diabetes less than 1 yr, 34% of the patients had duration of diabetes less than 2-5yrs and 12% of the patients between 6-10yrs. The average duration of diabetes in this study was 3.60yrs with standard deviation ± 4.20 .³ observed similar results as 42% of the patients had a duration of diabetes between 2-5 yrs , 32% of the patients had a duration of diabetes between 6-10yrs and in 22% of the patients ,duration of diabetes below 1 years. 4% of the patients had diabetes for more than 10years.

The fasting and postprandial blood sugar values showed a definite correlation with pulmonary tuberculosis. Mean fasting blood sugar value was

166.64 mg/dl and postprandial blood sugar was 247.88 and the difference was statistically significant when we correlated with lower lung field (p value < 0.05)⁴ in their study observed similar results as 44% of the patients had fasting blood sugar values between 201 to 300 mg/dl, 24% had values between 151 - 200 mg/dl and 18% of the patients had values above 300 mg/dl.

Bilateral involvement was present in 32% while unilateral involvement was present in 68%. Ten patients out of the 50 had cavitory disease. Cavitory lesions were more frequently confined to lower lung field (80%). Nodular lesions were found in 36%, exudative lesions were found in 22%⁵ 2016 Radiological studies indicate that 'non-diabetic' TB affects upper lobes, with pulmonary infiltrates, cavitory lesions, and hilar or paratracheal lymphadenopathy, while 'diabetic' tuberculosis presents more extensive lesions, with a greater involvement of the parietal pleura and a multilobar involvement, with confluent lesions and more frequently cavitory leision

In the study by cavitory lesions were noted in 52.88% of patients. 27.14% of patients had infiltration. Fibrosis was noted in 30% of patients. Lower lung field involvement was noted in 25.71% of patients and was more common in patients greater than 50 years. Multiple cavities and multiple lobe involvement are more common in tuberculous diabetics and lower lung field is involved more commonly in older age group patients. Severe hyperglycaemia appears to be a contributory factor to the development of pulmonary tuberculosis in diabetics. Diabetes appears to have no effect on the presenting features of pulmonary tuberculosis to a large extent. This was similar to our observation.

In this study, There were co-morbidities present like CVA with IHD(4%), Uraemia with DM Nephropathy (6%), Hydropneumothorax (4%), DM with DKA(4%).

Conclusion:-

The burden of diabetes mellitus and tuberculosis is increasing in developing countries especially in India. The current diabetic epidemic may thus leads to resurgence of tuberculosis in a TB endemic region like India .So ,screening of TB patients for Diabetes and regular watch for Tuberculosis infection in Diabetes, may help us to diagnose tuberculosis and diabetes earlier, thus enabling better outcome.

As tuberculosis in Diabetes presents with atypical clinical presentation like paucity of symptoms, atypical radiological finding like cavitation and lower lung field involvement and sputum for AFB negativity may result in late diagnosis or misdiagnosis. This may lead to increased morbidity and mortality.

Hence ,just as in HIV coinfectd with TB, one should have a high index of suspicion in cases of diabetes who develop cough ,fever of even one or two days duration. Early suspicion and screening of diabetes in tuberculosis and vice versa will lead to reduce tuberculosis burden and diabetic complications, which will also help to decreased economic burden on family and country, as tuberculosis affect most economically productive age group.

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