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Examination of the Glycemic Profile of Pulmonary TB Patients

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ABSTRACT

Background: Diabetes has long been recognised as a risk factor for both current and reactivated tuberculosis (TB). Diabetes increases the risk of tuberculosis by a factor of three (TB). Consequently, the incidence of tuberculosis is higher among diabetics than in the general population, and diabetes is a common comorbidity in TB patients. There is scientific evidence linking the two disorders, as indicated by systematic reviews. Diabetes and TB may exacerbate one another on multiple ways.

Aims & objectives: To examine the glycemic profile of pulmonary TB cases that are active

Methods & Materials: Department of Medicine, Santosh Medical College & Hospital, Ghaziabad, Uttar Pradesh, was where the research was conducted. Outpatients and inpatients of the medicine department at Santosh Hospital in Ghaziabad, Uttar Pradesh. Included in the study were a total of 100 consecutive cases of active pulmonary TB and 30 age- and gender-matched healthy controls.

Results: Poor glycaemic control and Co-morbid diabetes was seen in 15% cases of TB as compared to 0% controls ($p<0.01$).Urine sugar was seen in 21% cases of TB as compared to none in control group($p<0.01$).No significant association was observed between glycaemic control status andsputum AFB results in spot sample (p-0.544).No significant association was observed between glycaemic control status and sputum AFB results in morning sample (p-0.85).

Conclusions: In accordance with the new WHO End TB Strategy, we advise that greater efforts be made to integrate programmes for non-communicable and communicable diseases in order to increase the overall impact of disease control and prevention. In actuality, the exhaustive programme.Management of DM-TB should involve avoidance of DM, early identification of DM, and glycemic control. When both tuberculosis and diabetes are treated concurrently, good glycemic control may enhance health outcomes. If individuals with tuberculosis also have diabetes, therapeutic monitoring may need to be intensified.

Keywords: Diabetes, tuberculosis ,comorbidity , evidence ,exacerbate, hyperglycemic

1. INTRODUCTION

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To study tuberculosis (TB), a significant global public health challenge that primarily affects poor and vulnerable populations It is the major cause of disability-adjusted mortality.In many places of the world, especially in low- and middle-income nations, life expectancy is increasing (2)Each year, almost 9 million people contract this infectious disease, andIt kills nearly to 2 million people annually.(1) In 2013, the World Health Organization (WHO) projected that 9.0 million people had tuberculosis, of which 2 million were from India (3,4). In addition, recent scientific research demonstrates the rising prevalence of diabetes in low- and middle-income countries (LMIC). According to the International Diabetes Federation (IDF), more than 371 million people across the globe have Diabetes Mellitus (DM) in 2012. (5). The World Health Organization predicts that diabetes-related fatalities would quadruple between 2005 and 2030. (6).In impoverished nations where tuberculosis is highly widespread, DM pandemic expansion has occurred.The rise is primarily attributable to dietary and physical activity modifications (7).

In the poorest countries, diabetes is more prevalent among the wealthy, but economic progress swiftly reverses this trend, such that persons from lower socioeconomic levels are more affected by diabetes; complications are more severe among the poor in all nations (8). Consequently, poorer socioeconomic groups are more susceptible to both diseases (9). Countries with low to middle incomes, such as India and China, that are witnessing the fastest increase in diabetes prevalence and have the largest burden of tuberculosis are believed to be affected by the twin epidemics of diabetes and tuberculosis. (10)2 Diabetes has long been known to be a risk factor for active TB and reactivation of \slatent TB. Diabetes increases the risk of tuberculosis by a factor of three (TB). Consequently, the incidence of tuberculosis is higher among diabetics than in the general population, and diabetes is a common comorbidity in TB patients. There is scientific evidence linking the two disorders, as indicated by systematic reviews. Diabetes and TB may exacerbate one another on multiple ways. Additionally, it is linked to worse TB treatment outcomes. Additionally, TB infection can exacerbate glycemic control. Interactions between medications might further complicate the situation, reducing the efficacy of both TB and diabetes therapies and perhaps exacerbating their negative effects. The presence of diabetes mellitus can produce a rise in blood glucose levels, and chronic hyperglycemic levels can have a deleterious effect on the presentation and prognosis of tuberculosis, decreasing the likelihood of a favourable outcome and raising the risk of relapse and death. (11,12)

Diabetes may potentially hasten the establishment of drug-resistant tuberculosis, particularly multidrug-resistant TB (defined as strains of TB resistant to both rifampin and isoniazid) in TB patients (13). In contrast, tuberculosis may precipitate the onset of diabetes and decrease glycemic control in patients with diabetes. TB medications may interfere with the treatment of diabetes due to drug interactions, and diabetes may affect the efficacy of certain anti-TB drugs (14).

National TB control programmes worldwide have implemented DOTS and the Stop TB Strategy with clear success over the past two decades, including large increases in case detection rates and improved treatment results (1). However, enhancements are still required to address the following obstacles:3 Countries must assure thorough and early detection of all kinds of tuberculosis; but, in the majority of nations, lengthy diagnostic and treatment delays persist.

Although the global percentage of treatment success has exceeded the aim of 85 percent, treatment outcomes are poor in many situations and for particular subpopulations (1).

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Reasons for frequent bad treatment outcomes may include poor adherence to therapy, a high prevalence of drug-resistance, and/or vulnerability associated with co-morbidities such as HIV, malnutrition, alcohol dependence, smoking-related diseases, and diabetes.

Although global TB incidence, prevalence, and mortality rates are decreasing, the rate of decline is significantly slower than anticipated (1).

The relationship between diabetes and tuberculosis has possible ramifications for each of the aforementioned obstacles to TB control. First, considering that patients with diabetes are at increased risk for tuberculosis, screening for TB in populations with high TB prevalence may be justified in order to improve early case detection. Second, because diabetes may raise the likelihood of unfavourable treatment results in tuberculosis patients, particular care may be required to ensure that people with diabetes receive high-quality TB treatment. This needs diabetes screening among TB patients in situations where underdiagnosis of diabetes is prevalent. Thirdly, widespread primary and secondary prevention of diabetes will aid in population-level TB prevention. Lastly, TB preventive medication may be required for individuals with diabetes who have recently been exposed to TB. (11)

The World Health Organization (WHO) and the International Union against Tuberculosis and Lung Disease (IUATLD) have developed a collaborative framework for the care and control of diabetes and tuberculosis that emphasises the routine implementation of four bi-directional screenings for both diseases. It strongly advises diabetes surveillance among TB patients in primary care settings in all countries. Screening for diabetes in tuberculosis patients can not only assure early case detection, but also improve diabetes treatment. Patients with tuberculosis who attend healthcare centres for directly observed treatment, short-course (DOTS) therapy could also receive diabetes management services. Consequently, both the patient and the health system would incur lower costs, and wasteful duplication of service delivery would be avoided. Co-located DOTS centres and diabetes clinics at the primary health clinic (PHC) level will represent a significant advancement in the early detection and management of these two diseases. (15)

Diabetes was uncommon throughout Osler's lifetime. The majority of diabetes cases occurred between the third and sixth decades, when the distinction between juvenile-onset and adult-onset diabetes did not exist. However, there was no mention of his textbook did not contain any relation between TB and diabetes.

Since the early 20th century, clinicians have seen a correlation between DM and TB, however they were frequently unable to determine whether DM caused TB or whether TB produced the clinical presentation of DM. During the middle of the 20th century, a few papers documented this correlation and speculated on its relevance.

Patients presenting with a cough lasting two weeks or more, with or without constitutional symptoms such as fever, weight loss, and loss of appetite, are subjected to two sputum smear examinations. One sample is taken in the early morning, while the other is a spot sample. If either 1 or both are true are positive for AFB, the patient is diagnosed with sputum smear-positive TB and anti-tuberculosis treatment (ATT) is initiated. Patients with two negative smears should get symptomatic treatment and broad-spectrum antibiotics for ten to fourteen days. Antibiotics that are effective against tuberculosis, such as fluoroquinolones (Ciprofloxacin, Ofloxacin, etc.), Rifampicin, and streptomycin, should not be administered under such circumstances.

If the patient does not have tuberculosis, he or she is likely to improve. If the symptoms persist, patients should undergo a second sputum smear examination (2 samples). If one or

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more smears are positive, the patient is diagnosed with positive sputum smear pulmonary tuberculosis. If none of the repeat sputum specimens are positive, a chest X-ray is performed, and if the x-ray results are compatible with pulmonary tuberculosis, the patient is diagnosed as sputum smear-negative pulmonary tuberculosis. And if the x-ray results are not suggestive of tuberculosis, it is preferable to investigate other non-TB reasons. Interferon gamma (IFN) Release Assay assesses T cell release in response to stimulation with ESAT-6 and CFP-10, which are highly TB-specific antigens. The T SPOT TB test is an enzyme linked immunospot assay (ELISpot), whereas the QuantiFERON TB Gold test is an ELISA for measuring Interferon gamma (IFN) in whole blood.The principle of treatment for tuberculosis (other than confirmed drug-resistant strains) shall henceforth be the administration of daily fixed dose combinations of first-line anti-tuberculosis medications in suitable weight ranges. (20)

Daily regimen fixed dose combination TB medications are packed to cover four weeks of treatment, or 28 days, and are delivered daily. Therefore, the patient would receive a total of 28 effective dosages every month.Treatment for a new TB case will last six months (24weeks). The intensive phase (IP) will consist of eight weeks of daily Fixed Dose Combinations of Isoniazid, Rifampicin, Pyrazinamide, and Ethambutol in four weight bands. There will be no requirement for IP extension. Only Pyrazinamide will be discontinued during the Continuation Phase (CP), while the other three medications will be administered daily for an additional 16 weeks. The CP can be extended by 12 to 24 weeks in specific kinds of tuberculosis, such as CNS TB, Skeletal TB, and Disseminated TB, based on the treating physician's clinical judgement.The treatment for previously treated cases of tuberculosis will last eight months (32 weeks).

As hyperglycemia may return after TB therapy, it is crucial to confirm glucose intolerance after TB cure. Even after the return of normal blood sugar levels, it has been demonstrated that continued monitoring is important.

Diabetes is a major predictor of impaired fasting glucose (10,13). Due to these factors, some propose screening at both the time of TB diagnosis and three months after treatment initiation (20).

In numerous investigations, the number of TB patients required for screening to detect one additional case of DM ranged from 4 to 54. Consequently, screening for DM in TB patients is more cost-effective than screening for TB in DM patients.

2. MATERIALS AND METHODS

The study was conducted in Department of Medicine, Santosh Medical College & Hospital, Ghaziabad, U.P.Outpatients and inpatients of department of medicine, Santosh Hospital, Ghaziabad, U.P. A total of 100 consecutive cases of active pulmonary tuberculosis coming in our

department and 30 age and sex matched healthy controls were included in the study.

Minimum of 100 fresh cases of active pulmonary tuberculosis, meeting the inclusion and exclusion criteria were included in the study. Informed consent was taken from these subjects. All the subjects were then followed up as given below: Detailed history was taken including total duration of illness, symptoms of fever, cough, expectoration, hemoptysis, chest pain and dyspnea and smoking habit, Relevant investigation were carried out including Hemogram, ESR, RFT,LFT,Serum protein, Urine examination, X-ray chest and Mantoux test.Sputum for AFB was done (2 samples) by Ziehl–Neelsen staining before starting anti

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tubercular treatment.,X-ray chest PA view was done., Glycosylated hemoglobin (HbA1C), FBG and the standard 75 grams 2 hour oral glucose tolerance test(OGTT) was done at the time of registration of the patient.Above mentioned investigations along with oral glucose tolerance test and glycosylated hemoglobin (HbA1C) was also done in 30 normal healthy volunteers matched for age, sex and socio economic status to establish normal standards The quantitative data will be represented as their mean ± SD. Categorical and nominal data will be expressed in percentage. The t-test will be used for analyzing quantitative data, or else non parametric data will be analyzed by Mann Whitney test and categorical data will be analyzed by using chi-square test. The significance threshold of p value will be set at <0.05. All analysis will be carried out by using SPSS software version
21.

3. RESULTS

The study included 100 cases of TB along with 30 controls (Non TB subjects).

Table 1: Comparison of study groups as per Gender

Sex	Group		Total
	Cases	Controls	
Female	50	9	59
	50.0%	30.0%	45.4%
Male	50	21	71
	50.0%	70.0%	54.6%
Total	100	30	130
	100.0%	100.0%	100.0%
p- value - 0.062			

Equal gender prevalence was seen in TB cases while male predominance was noted in controls. The gender difference between groups is however non-significant

Table 2: Comparison of study groups as per Blood Investigations

Blood SugarIndices	Group	N	Mean	SD	p- value

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FBS	Cases	100	104.84	24.15	<0.01
	Controls	30	87.67	6.66	
1st Hour	Cases	100	176.99	32.29	<0.01
	Controls	30	121.23	9.18	
2nd Hour	Cases	100	136.28	32.17	0.33
	Controls	30	142.10	7.89	
HbA1c	Cases	100	6.76	0.55	<0.01
	Controls	30	6.06	0.29	

Mean Hemoglobin and Platelet levels were significantly higher in TB cases as compared to controls ($p<0.05$) while mean ESR was significantly higher (45.5 vs 13.5; $p<0.01$).

Table 3: Comparison of study groups as per Glycaemic control

HbA1c Levels	Group		Total
	Cases	Controls	
< 6.5%	36	30	66
	36.0%	100.0%	50.8%

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6.5%- 8.5%	64	0	64
	64.0%	0.0%	49.2%
Total	100	30	130
	100.0%	100.0%	100.0%
p- value < 0.01			

Poor glycaemic control was associated with TB cases with 64% cases having HbA1c levels over 6.5% compared to none in control group (p<0.01).

4. DISCUSSION

Global consequences of the interaction between diabetes mellitus and tuberculosis are compounded by the fact that there is global epidemic of diabetes mellitus. Prevalence of diabetes mellitus is expected to rise from 370 million in 2012 to more than 500 million by 2030. Diabetics are four to five times more prone to contract tuberculosis than the general population.

Since the risk of developing TB is more likely in diabetic patients, this correlation between diabetes and TB could have a negative impact on TB control programs.(18) With following rationale in mind, this study was conducted to estimate the glycemic profile in newly diagnosed cases of TB and determine various socio demographic and clinical factors that may be associated with the same retrospectively. It was a Case control study conducted in the Department of Medicine, Santosh Medical College & Hospital, Ghaziabad, UP. 100 fresh cases of active pulmonary tuberculosis and 30 normal healthy volunteers taken as controls, matched for age, sex and socio economic status to establish normal standards were included in the study.

The diabetes epidemic is rapidly increasing in many countries, with the documented increase most dramatic in low- and middle-income countries. The global prevalence of diabetes among adults over 18 years of age has risen from 4.7% in 1980 to 8.5% in 2014.India had 69.2 million people living with diabetes (8.7%) as per the 2015 data. Of these, it remained undiagnosed in more than 36 million people.(15)

The prevalence of diabetes in TB patients in these study is seen to be much higher than the prevalence seen in the general population. This can be attributed to living in an urban environment (metropolitan cities) and aged 50 years and above. Urban residence may indicate lifestyle practices that predispose to DM or better access to diagnosis of DM in urban settings, which is also supported by ―The Indian Council of Medical Research (ICMR)‖

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study conducted in the 1970s reported a prevalence of 2.3% in urban areas; this number has risen to 12%-19% in the 2000s.(128) Correspondingly, in rural areas, prevalence rates have increased from around 1% to 4%-10% and even 13.2% in one study. Thus, it is clear that both in urban and rural India, prevalence rates of diabetes are increasing rapidly with a rough urban/rural divide of 2:1 to 3:1 being maintained through the past 2 to 3 decades(19)
Diagnosis of DM was based on the estimation of HbA1c levels and confirmed byfastingblood glucose (FBG) and 2hour post prandial blood sugar levels in present study. 64 of the freshly diagnosed TB [20-22]cases had HbA1c levels between 6.5-8.5% on initial investigations, out of which 15 were later confirmed as Diabetic cases by oral FBG and the standard 75g 2 hour oral glucose tolerance levels (OGTT).This may be due to some technical error or some biochemical reaction between mycobacterium tuberculosis and glycosylated haemoglobin which further needs to be studied.

Present study also observed significantly higher rates of positive sputum and higher sputum mycobacterial load in patients with poor glycemic controls as compared to those with good glycemic control patients.[24-26] This study has shown a high prevalence of DM in patients with active TB, and supports routine screening of TB patients for DM and diabetic patients especially those with poor glycemic status should be screened regularly for tuberculosis. So that both the diseases can be detected early and treated promptly.

5. CONCLUSION

Diabetes Mellitus is a major risk factor for TB and will likely be an important driver of TB epidemiology in the upcoming decades. Our study attempted to explore the prevalence of diabetes in newly diagnosed pulmonary TB patients. The prevalence of Diabetes was found to be higher in newly diagnosed pulmonary TB patients thus indicating the need for intensified bidirectional screening. Present study highlighted the interplay of TB and DM as an emerging health care challenge in low and middle income countries. This has potentially serious implications for tuberculosis control, and it must become a priority to use this knowledge to initiate focused and coordinated action like active case finding, treatment of latent tuberculosis and new research in parts of the world where diabetes is epidemic and TB endemic to properly inform public health and clinical practice.

Echoing the new WHO End TB Strategy, we urge that more efforts be made to link non-communicable and communicable disease programs in order to leverage the overall impact on disease control and prevention. In practice, the comprehensive program for DM-TB management should include prevention of DM, early detection of DM followed by proper glycemic control. Good glycaemic control might improve health outcomes when tuberculosis and diabetes are simultaneously treated. Tuberculosis treatment monitoring might need to be more intensive if patients with tuberculosis also have diabetes.
Additionally, other interventions should be considered, especially for patients with newly diagnosed diabetes and for people who need insulin. More evidence is needed to support screening and subsequent treatment for latent tuberculosis infections in patients with diabetes. Integration of health services could result in better tuberculosis prevention, 77 an early diagnosis and start of treatment for diabetes, and improved care for concomitant disease. However, the practical and economic implications need further assessment.

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