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Research Article

Tuberculosis and diabetes: the deadly duo

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ABSTRACT

Background: With diabetes on the rise globally and with enormous pools of latent TB infection and high burdens of active disease in many countries, tuberculosis-diabetes is a looming co-epidemic. Furthermore, in countries where diabetes is escalating and tuberculosis rates are already high, diabetes will increasingly impede efforts to control tuberculosis.
Methods: A prospective study including fifty diabetic and fifty non diabetic sputum positive pulmonary tuberculosis patients was conducted for a period of one year. Thorough clinical examination, relevant investigations like blood sugars, chest X-ray, and smear for acid fast bacilli were done and results analyzed statistically.
Results: Though there is no significant difference in the clinical symptoms in both the groups, diabetic tuberculosis patients have prominent clinical severity at the onset, a greater degree of lung involvement and residual changes. There is predominance of lower zone involvement (56%) in diabetic patients and upper and mid zone involvement in non-diabetics. Extensive bilateral lesions and cavitations were more in diabetic patients. Sputum negativity after completion of intensive phase treatment was lower in diabetic patients compared to non-diabetics. Patients on insulin have better sputum conversion (94%) in comparison with oral hypoglycemic agents (76%). Relapse rate was high in diabetics (23.3%) compared to non-diabetics (8%).
Conclusions: Diabetes mellitus is growing rapidly worldwide and is increasingly fueling the spread of tuberculosis. Atypical presentations like lower lung field involvement and cavitations were common. Strict glycaemic control enhances the sputum clearance and results in better patient outcome.

Keywords: Acid fast bacilli, Diabetes mellitus, Oral hypoglycemic drugs, Lower lung filed tuberculosis

INTRODUCTION

Since ancient times, physicians have been aware of the association between tuberculosis and diabetes mellitus; perhaps the earliest to note it was the great Indian physician Susruta, in 600 A.D.[1] Experts have raised concern about the merging epidemics of tuberculosis and diabetes particularly in the low to medium income countries like India. In these, populace the incidence of tuberculosis is raising due to high rates of infection with HIV, high prevalence of malnutrition and crowded living conditions, or poor tuberculosis control infrastructure. At the same time, diabetes mellitus prevalence is soaring globally, as a consequence of increases in obesity, changing patterns of diet and physical activity, and aging populations. There is growing evidence that diabetes mellitus is an important risk factor for tuberculosis and might affect disease presentation and treatment response. Furthermore, tuberculosis might induce glucose intolerance and worsen glycemic control in people with diabetes.[2] In the setting of the increasing overlap of populations at risk for both diseases, the combination of tuberculosis and diabetes mellitus represents a global health threat. Henceforth a clinical study was conducted

to evaluate the varied presentation and treatment response of pulmonary tuberculosis in diabetic peoples.

METHODS

A prospective study including one hundred microscopically proven cases of sputum smear positive pulmonary tuberculosis from January 2014 to December 2014.Among these, 50 were diabetic and 50 were non-diabetic patients with sputum positive tuberculosis. A detailed history and through clinical examination were done. Investigation of fasting and prandial plasma glucose levels (FPG, PPG), complete urine examination were done on Rosche semiautomatic analyzer. Digital chest skiagrams were taken and interpreted by senior radiologist. Sputum smear for acid fast bacilli (AFB) by florescence staining was done in designated microscopy center and were graded accordingly.

RESULTS

A total of one hundred sputum smear positive patients including fifty diabetics and fifty non-diabetics were studied. The mean age of presentation for diabetics is 46years and for non-diabetics 35 years. Males affected are twice the number of females in both diabetics and non-diabetics. There is no significant difference in the clinical symptoms in both the groups and include fever (95%), productive cough (77%), dyspnoea (50%), hemoptysis (35%), chest pain (30%), and polyuria (30%) and weight loss (25%).

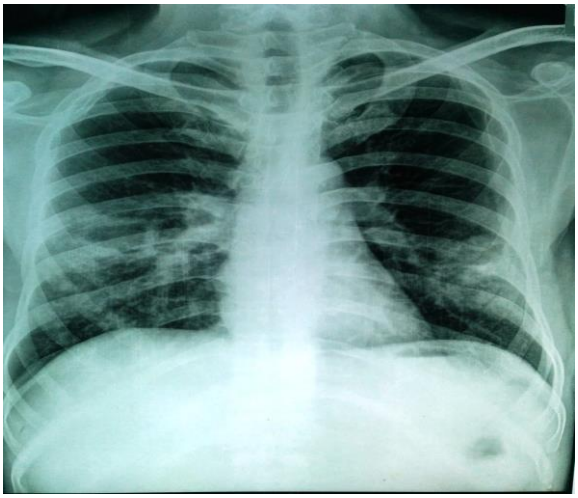

Figure 1: Chest X ray PA view showing bilateral lower zone infiltrates with cavitation (S/o Lower lung field tuberculosis).

There is predominance of lower zone involvement in diabetic patients (56%) and upper zone involvement in non-diabetics (60%) (Figure-1). The number of pleural effusions also was more in diabetic group (14%). Among diabetic patients: Lower zone – 56% (n=28), Upper zone-8% (n=4) and mid zone –12% (n=6).Among non-diabetic patients: Upper zone – 60% (n=30), mid zone -8% (n=4) and lower zone -10% (n=5), (Figure-2).

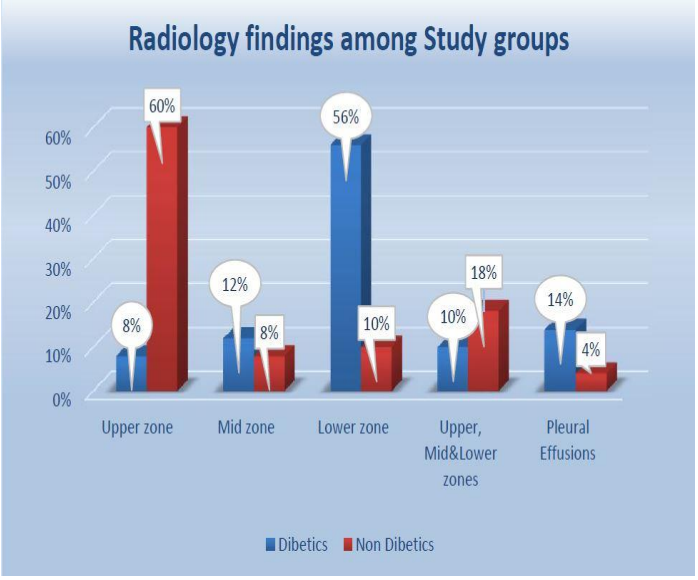

Figure 2: Zonal involvement on chest X-ray among diabetics and non-diabetic tuberculosis patients.

The incidence of multilobar and bilateral lesions is more in diabetic patients compared to non-diabetics. There are more cavitary lesions in diabetic patients (40%) compared to non- diabetics (24%). Fungal colonisation also seen infrequently (Figure-3).

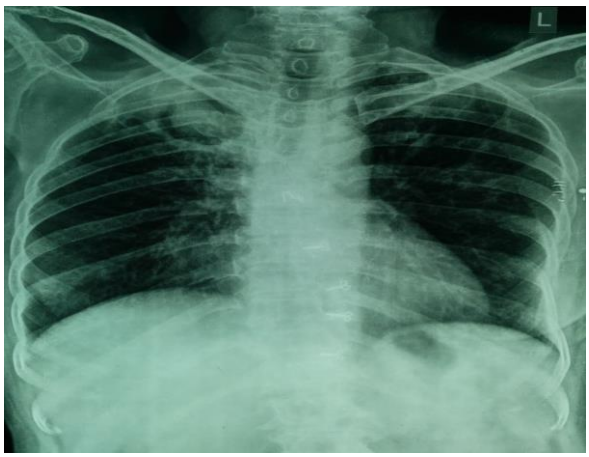

Figure 3: Chest X ray PA view showing right upper lobe fungal ball.

The pre-treatment bacillary load was more for diabetic patients compared to non-diabetics. At the end of two months intensive phase sputum conversion rates were significantly lower in diabetic patients (64%) compared to non-diabetics (88%).

Treatment outcome: Patients on insulin have better sputum conversion to negativity (82.5%) at the end of 2nd month in comparison with oral hypoglycemic agents (37.5%). There is no relationship with duration of diabetes with sputum conversion (Figure-4).

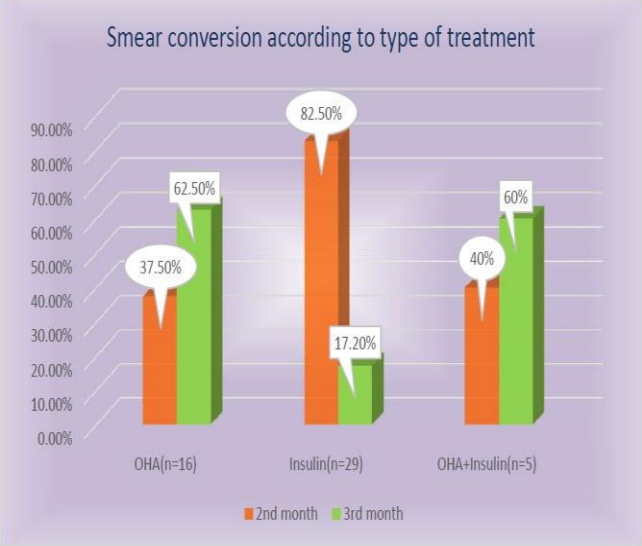

Figure 4: Comparison of sputum smear conversion between insulin and oral hypoglycemics.

DISCUSSION

As a destroyer of mankind, tuberculosis has no equal. An estimated nine million fell ill with TB in 2014 and 1.5 million died worldwide.[3] About one in three people worldwide live with a latent TB infection. In most cases this infection will remain dormant for one's entire life, never making the person sick. However, the risk that this latent infection will progress to active TB disease increases significantly if a person's immune system is compromised as in diabetes. Tuberculosis has already been declared a "global emergency" by the WHO[4], now with diabetes assuming epidemic proportions it is imperative to take measures for the prevention and control of this deadly duo.

Diabetes was estimated to increase the risk of tuberculosis from 1.5 to 7.8 fold.[5] Diabetes is associated with a decrease in cellular immunity. There are fewer T lymphocytes and a decreased neutrophil count in diabetics. A reduced T-helper1 (Th1) cytokine response level, TNF alpha production, and IL-1beta and IL-6 production is also seen amongst people with concomitant diabetes and TB as compared to non-diabetic individuals.[6] Th1 cytokines are vital in the control and inhibition of mycobacterium tuberculosis bacilli. Macrophage function is also inhibited in individuals with diabetes, with an impairment of the production of reactive oxygen species, and phagocytic and chemotactic function. Hyperglycemia has a direct depressive effect on the respiratory burst. A combination of these dysfunctional processes contributes to an increased risk of TB in diabetes.[7]

The relationship between DM and TB is bi-directional. There is high prevalence of impaired glucose tolerance as a response to acute severe stress in patients with tuberculosis.[2] Fever, protracted inactivity and malnutrition stimulate the stress hormones epinephrine, glucagon, cortisol and growth hormone, which acting synergistically raise the blood sugar levels. Plasma levels of IL-1 and TNF alpha are also raised in severe illness which can stimulate the anti-insulin hormones. Age, co-existent illnesses and alcoholism also influence the host response. Higher incidence of chronic calcific pancreatitis also noted in patients with concomitant diabetes and tuberculosis leading to insulin deficiency.[8] In most of these cases, the impaired glucose tolerance reverts back to normal after successful treatment for TB; however the increased risk of developing diabetes persists.

According to various studies, age of presentation differs from general population with diabetic present at an increasing age. In our study the mean age of presentation for diabetics is 11 years later than non-diabetics with tuberculosis. Studies have shown that Indians are inherently more insulin resistant compared to otherworld population groups and develop diabetes at a younger age. Westernization of diets, adoption of lifestyles that are more sedentary and urbanization are all suggested cofactors in the epidemic of DM in India.

Despite the fact that there is no noteworthy distinction in the clinical manifestations in both the groups, diabetic tuberculosis patients have more prominent clinical seriousness at the onset, a greater level of lung involvement.[9] It is worthwhile to mention that both these diseases may simulate the symptoms of the other. Such symptoms that are common to both include lethargy, fatigue, weight loss, fever and loss of appetite. It is not unheard of for people with diabetes to present to the doctor with complaints of worsening of blood glucose control only to find out later that they have TB. The diabetic tuberculosis patients may also frequently develop complications like coma and diabetic microangiopathies.[10]

Sosman and Steidl reported that "diabetic tuberculosis" has a special radiological pattern consisting of confluent, cavitary, wedge shaped lesions spreading from the hilum towards the periphery, predominantly in lower zones.[11] They tend to be more aggressive, bilateral and associated with pleural effusion. Lower lung field tuberculosis is defined as "tuberculosis disease found below an imaginary line traced across the hilar and including the parahilar regions on a standard posterior-anterior chest roentgenogram". The cause of lower lung field tuberculosis is transbronchial perforation of a hilar lymph node, with spread to the adjacent lung. Thus, lower lung field disease occurs as a continuation of the primary tuberculosis infection or soon afterwards in the post primary. This explanation is consistent with the high incidence of endo-bronchial involvement. Other mechanisms postulated in the pathogenesis of lower lung field tuberculosis have been restricted ventilation, costal breathing, and retrograde lymphatic flow from involved hilar nodes. Consolidation in lower lung field disease tends to be more confluent and extensive than that found

in upper lobe disease. Marias observed lower lung field tuberculosis in 29% of patients with diabetes, as compared to 4.5% in the non-diabetic patients.[12] Lower lung filed TB was noted in 60 % of diabetics and in 15 % of non-diabetics in this study.

Diabetic tuberculosis patients have higher pre-treatment bacillary load because of profound immune suppression. At the end of two months intensive phase, sputum conversion rates were significantly lower in diabetic patients compared to non-diabetics.[13] Sputum negativity is increased if intensive phase drug therapy extended for one more month.

Diabetes may have a negative impact on the outcome of TB treatment: higher failure rates, higher rates of all-cause mortality and death specifically related to TB.[13] Some explanations for worse outcome are higher rates of drug resistance, impaired cellular immunity, delay in sputum conversion and lower plasma levels of anti TB drugs. The high drug resistance in diabetes is attributed to hyperglycemic status which may interfere with achieving adequate tissue levels of medications or might interfere with alveolar macrophage or CD4+ cell function. Rifampicin as a potent hepatic microsomal inducer induces the metabolism of biguanides & sulfonyl ureas and decreases their efficacy.[14] Diabetes also alters the pharmacokinetics of several anti-TB drugs. The altered plasma levels may be due to differences in absorption, distribution, metabolism and/or excretion in diabetics.[15] Lower plasma levels of anti-TB drugs are associated with resistance to these drugs which may complicate the course of treatment of TB in people with diabetes. A relapse rate of 23 % seen in diabetics in the present study. Many studies have found an increased risk of multidrug resistant tuberculosis (MDR-TB) among diabetics, ranging from 2.1 to 8.8 times morecommon.[16]

Management of DM in TB should be aggressive. An optimal glycemic control results in a better patient outcome.[17] Insulin therapy should be initiated at the outset, using basal bolus regime or premixed insulin. Insulin requirements are high to begin with but fall after a few weeks once hyperglycemia is corrected and infection is controlled. In patients with co-existing peripheral neuropathy due to diabetes, it is mandatory to give the patient pyridoxine if isoniazid is to be used.[18] Once optimal glycemic levels are achieved, therapy can be shifted to oral hypoglycemic drugs. Screening for DM in patients with TB could improve case detection, early treatment, and prevention of DM complications.[19]

CONCLUSIONS

Diabetes is rampant affecting the poor and rich alike, and increasing the risk of tuberculosis across all population segments. Both diseases are linked with each other, and need to be treated together for optimal outcome. Providing regular bi-directional screening for the two diseases will prevent them early in course. It is within our power to respond to the looming TB-diabetes co-epidemic and forestall its most harmful consequences.

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