ORIGINAL ARTICLE

A STUDY ON DIABETES MELLITUS AMONG CASES OF PULMONARY TUBERCULOSIS IN A TERTIARY CARE HOSPITAL, AHMEDABAD

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ABSTRACT

Introduction: Tuberculosis and Diabetes mellitus are two public health problems which not only often coexist but have serious implications on each other.DM has an impact on symptomatology,radiological manifestation,diagnosis,and management of TB.TB has significant impact on DM,causing unmasking of DM and poor control because of stress or because of drug treatment for TB.Present study attempts to asseses this coexistence with regard to the age predisposition,sex preponderance, duration and glycemic control of diabetes and the radiological manifestation.

Methodology: 84 patients presenting to Pulmonary Medicine Department Smt N.H.L Municipal Medical College, Ahmedabad who were suffering from both Tuberculosis and Diabetes mellitus, were studied. Various parameters considered included age, sex, history of diabetes with regard to the duration and glycemic control and radiological presentations.

Results: It was found that majority were males(52 /84).The age group most commonly involved was the 40-60 year group (64 /84).Majority had their diabetes diagnosed before diagnosis of tuberculosis (48 /84), 19 had diagnosis after TB diagnosis .Out of these 48 diagnosed diabetes,9 had controlled diabetes whereas 39 had uncontrolled diabetes.26 patients had the typical radiological lesions while 58 had atypical radiological manifestation with either patchy opacity or cavitations fanning out from hilar region, lower lobe involvement and multi lobe involvement.

Conclusion: TB and DM often coexist together and adversely affect eachother.Both need to be managed properly in order to achieve favorable treatment outcome.

Key Words: Tuberculosis, Diabetes Mellitus, Co-infection

INTRODUCTION

Globally, there are 7 billion people estimated to be living in the world. Tuberculosis (TB) remains a major cause of mortality in developing countries. Incidence of TB is greatest among those with conditions impairing immunity [1] such as human immunodeficiency virus (HIV) and diabetes. The most recent estimates of the global burden of diabetes mellitus (DM) come from the 2012 Diabetes Atlas of the International Diabetes Federation [2]. In 2012, there were an estimated 371 million cases of DM globally, and by 2030 it is expected that this number will have risen to 552 million. 80% of people with DM live in low- and middle-income countries and 50% of all people with DM (183 million) are undiagnosed. It is estimated that DM caused 4.8 million deaths in 2012. In South East Asia Region, more than 70.3 million people have diabetes; by 2030 this will rise to 120.9 million and 8.7 % of adults in the South East Asia Region have diabetes. Nearly one fifth of all adults living with diabetes, live in this region. As a consequence of urbanization as well as social and economic development, there has been a rapidly growing epidemic of diabetes mellitus (DM) [2,4]. Available data suggest that an estimated 11% of urban people and 3% of rural people above the age of 15 years have DM. Among them about half in rural areas and one third in urban areas are una-

ware that they have DM. Most recent estimates from the International Diabetes Federation put the number of persons with diabetes mellitus at 63 million (~10% of the adult population), with a further 77 million having impaired glucose tolerance.

India is a country with 1.2 billion people (or 17.5% of the world population). India has the largest number of TB cases in the world (estimated at 2.0 million per annum) with an incidence rate of 168/100,000 per year for 2009 [3]. The national case detection rate for new smear positive cases was 71% in 2012. Treatment success for new smear-positive pulmonary TB cases for the cohort in 2009 was 88%, slightly higher than the global average. In India diabetes prevalence is increasing rapidly. Diabetes increases the risk of TB. Diabetes mellitus (DM) significantly contributes to the burden of incident TB cases. In a study in India, DM accounted for 14.8% of pulmonary TB and 20.2% of smear positive TB. [5] It has also been postulated that transitory changes in carbohydrate metabolism in patients with DM may lead to persistent hyperglycemia, increasing chances of development of TB.The global burden of diabetes is increasing; recent estimates highlight the importance of this disease in India. There were an estimated 20-30 million people in India with diabetes in 2000 (estimates vary with study methodology) [6, 7] and projections suggest prevalence will rise to almost 80 million people by2030. The co existence of these two conditions has serious implications with regards to the clinical presentations and radiological findings, the management and the final treatment outcomes. [7]

OBJECTIVES

The objectives of the study were to assess the feasibility and results of screening diabetes (DM) for pulmonary TB and TB patients for DM within routine health care setting; and to assess this coexistence with regard to age predisposition, sex preponderance, duration and glycemic control of diabetes and radiological presentations.

METHODOLOGY

The epidemiological and clinical interactions between TB and DM are similar to those observed between TB and HIV. The impact of these interactions, though different in magnitude at the individual level may even out at the population level due to the higher prevalence of DM in the population. The similarity of interactions provides an opportunity for application of lessons learnt in TB-HIV collaboration to TB-DM collaboration as well. The screening for active TB in DM patients is followed as per the guidelines of the Revised National TB Control Programme (RNTCP).The screening for DM in Tb patients followed the guidelines stipulated by the National Programme for prevention and control of Cancer, Diabetes, Cardiovascular Diseases and stroke (NPCDCS) in India.84 patients presenting to the Pulmonary Medicine Department, Smt.N.H.L Municipal Medical College, Ahmadabad, who were suffering from both TB and DM, were studied.Various parameters considered included age, sex, history of diabetes with regard to duration and the glycemic control and the radiological presentations.

RESULTS

It was found that majority were males (52 /84). The age group most commonly involved was the 40-60 years group (64 / 84)

Majority had their Diabetes diagnosed before the diagnosis of Tuberculosis (48 /84), 19 had diagnosis after TB diagnosis, and 17 simultaneously with TB diagnosis.

Table 1: Relation between diagnosis of DM and TB

Disease	Cases
Diabetes before TB	48(57.14%)
Diabetes with TB	17(20.24%)
TB before Diabetes	19(22.62%)

Table 2: Relation between treatment and control of DM with TB

Treatment and control of DM with TB	Frequency(%)
Regular treatment and Controlled DM	9(18.75)
Irregular OHA's and Uncontrolled DM	29(60.42)
Alternate system of Medication and Uncontrolled DM	3(6.25)
Regular treatment and Uncontrolled DM	7(14.58)

Table 3: Radiological features

Radiology	**Frequency (%)**
Typical	26(30.95%)
Atypical	58(69.05%)

Table 4: Atypical radiological features

Radiological features	Frequency (%)
Fanning out from hilum	9(15.52)
Lower lobe involvement	28(48.28)
Pneumonia like Picture	6(10.34)
Any combination	15(25.86)

Out of these 48 diagnosed diabetes, 9 patients had controlled diabetes whereas 39(81.25%) had uncontrolled diabetes. Out of these 29 were on oral irregular hypoglycemic, 3 on alternate system of medicine and 7 despite of having regular medication had uncontrolled diabetes. 26 Patients had the typical radiological lesions while 58 had atypical presentations.

The atypical radiological presentations were having either patchy opacities or cavitations fanning out from hilar region, lower lobe involvement and multi lobe involvement.

DISCUSSION

The Association of Tuberculosis and Diabetes has been studied since long. In 1964, Richard Morton's phthisis: or treatise on consumption stated the association even in Roman times. In the latter half of the 19th century, Root stated the diabetic patient appeared doomed to die of pulmonary TB if he succeeded escaping coma. Half century ago, expert clinics were established for "tuberculous diabetics". [8]

People with a weak immune system, as a result of chronic diseases such as diabetes, are at a higher risk of progressing from latent to active TB. Hence, people with diabetes have a 2-3 times higher risk of TB compared to people without diabetes. About 10% of TB cases globally are linked to diabetes.

A large proportion of people with diabetes as well as TB is not diagnosed, or is diagnosed too late. Early detection can help improve care and control of both diseases. All people with TB should be screened for DM particularly in settings with high DM prevalence.DM can lengthen the time to sputum culture conversion and theoretically this could lead to the development of drug resistance if a 4-drug regimen in the intensive phase of therapy is changed after 2 months to a 2-drug regimen in the presence of culture-positive TB.People with diabetes who are diagnosed with TB have a higher risk of death during TB treatment and a higher risk of TB relapse after completing treatment. WHO-recommended TB treatments should be rigorously implemented for a person with TB/DM.DM is complicated by the presence of infectious diseases, including TB. It is important that proper care for diabetes is provided to patients suffering from TB/DM.It has been argued that good glycemic control in TB patients can improve treatment outcomes. [9, 10, 11, 12, 13]

TB is a stressful condition which can worsen the dibetes can lead to the higher requirement of the anti diabetic agents. As per the correlation between the ventilation and perfusion, since the perfusion is more in the middle and lower lobes, TB bacilli find a more congenial environment for the growth in the glucose rich blood in uncontrolled diabetics.

Present study attempts to asseses this coexistence with regard to the age predisposition, sex preponderance, duration and glycemic control of diabetes and the radiological presentations.

Diabetes mellitus has found to be associated with progressive shift of male predominance in pulmonary tuberculosis [14] Yamagishi et al., also found a male predominance among 352 tuberculosis patients with diabetes.[15] Similar were the findings from our study showing male predominance(52 /84).Although the cause of this discrepancy is unclear, it possible that genetic or social-cultural difference among the populations might affect the way in which diabetes mellitus influences in gender distribution in pulmonary tuberculosis.

Swai et al prospectively followed 1250 African patients with Diabetes mellitus for several years. In 25.7% Tuberculosis was diagnosed prior to onset of Diabetes mellitus, and in45.7%, subsequently. In 20.6%, Tuberculosis and diabetes were diagnosed simultaneously. Our study was comparable to this study with majority of the patients having their Diabetes diagnosed before diagnosis of tuberculosis (48/84) 19 diagnosed after TB diagnosis, and 17 with TB diagnosis.

Prevalence of Tuberculosis was greater in those with poorly controlled Diabetes mellitus [16] in our study 39/48 =89.17% of the diagnosed diabetics were uncontrolled. They were on either irregular hypoglycemic or Insulin's or their diabetes was not controlled even after regular medications.

An increased susceptibility of patients with diabetes mellitus to develop tuberculosis could be due to neutrophil dysfunction & important cytokines production.[17] Interferon alpha producing capacity of WBC culture has been found to be reduced in patients of diabetes mellitus as well as tuberculosis patients.[17] Tsukaguchi et al [18] found a significant lowered production of IL-1ß & TNFa by peripheral blood monocytes in patients with tuberculosis and coexisting diabetes mellitus compared to patients with tuberculosis who do not suffer from diabetes mellitus. Production of IL-1ß & TNFa was significantly lower in patients with poor glycemic control.[18] Increased susceptibility to tuberculosis is also due to thickened alveolar epi-

thelium & pulmonary basal lamina, decrease pulmonary diffusion capacity, lung volume and elastic recoil in patients with diabetes mellitus. Pathogenesis of these changes is currently thought be due to non enzymatic glycosylation of tissue proteins inducing an alteration in connective tissue in diabetes mellitus.[19]This thickening in alveolar epithelium may decrease the bacillary growth because of lower oxygen availibilityfor TB bacilli . B andut the alveolar thickening may not be that much to lead on to sufficient falls in oxygen levels that decrease the growth. Or as earlier stated, the locally high glucose levels due to hyperglycemia may overpower this decrease oxygen content and become more significant to cause bacillary proliferation. Further diabetic autonomic neuropathy also leads to abnormal basal airway tone due to alteration in vagal pathway and thus causing reduced bronchial reactivity and bronchodilatation. [19]

The degree of hyperglycemia has been found to have a distinct influence on the microbicidal function of macrophages, with even brief exposures to blood glucose level of 200mg% significantly depressing the respiratory burst of these cells. [20, 21] This is borne out by the observation that in poorly controlled diabetics, with higher levels of glycoselated hemoglobin, tuberculosis follows a more destructive course and is associated with higher mortality.

Pulmonary tuberculosis occurs predominantly in lung apices. It has been suggested that in patients in with diabetes mellitus, tuberculosis occur predominantly lower lobe with frequent cavitory lesions. [22] In other studies also, cavitory disease and multi lobe involvement was found to be more common in patients with pulmonary tuberculosis and diabetes.[23]

However, in recent case control study, distribution of lesions including cavitory lesions was found to be similar in chest radiographs of tuberculosis patients with or without diabetes mellitus.[24] Our studies showed that 58 patients had atypical presentations with either lower lobe involvement,multi lobe involvement, cavitations or shadows fanning out from the hilum.The atypical images of pulmonary tuberculosis in diabetic patients have been vaguely attributed to an immune abnormality and perfusion differences. It is known that diabetes mellitus causes a decrement in the activity of lymphocyte and diminution in the number of monocytes and macrophages with abnormalities in their chemotactic and phagocytic activities.[18] Moreover, diabetes also produces dysfunction of polymorphonuclear leukocytes, with a reduction in their bactericidal activity.Whilist more research is needed to clarify the role of leucocytes, the 'premature aging' of the lung induced by diabetes seems to be the main factor responsible for the development of the 'atypical, radiological pattern.

CONCLUSION

The atypical radiological images like lower lobe involvement, fanning out from hilum or pneumonia like picture could mask the diagnosis of tuberculosis in diabetic patients, making the clinician think of diagnostic possibilities other than tuberculosis, with a consequent delay in the administration of proper treatment, causing far advanced or disseminated tuberculosis. Patients with TB and diabetes usually have uncontrolled diabetes. In patients of TB, diabetes may get unmasked because of the stress and infection and patients started on AKT with rifampicin containing regimens may require increased doses of oral hypoglycemic. In a patient of diabetes having poor control and symptoms suggestive of TB, TB should be suspected .Patients put on rifampicin containing regimens should have their oral hypoglycemic doses modified for proper glycemic control. To achieve the target level of control, the drugs rather than diet should be used. Also a high index of suspicion is required in reading the X-ray films, before making diagnosis, especially in immunocompromised states like Diabetes mellitus. Proper control of diabetes is important as it can act as a double edged weapon leading to pulmonary TB and delay in diagnosis because of atypical presentations. An important step in the fight against DM and TB has been the development of a WHO-Union Framework for collaborative activities to guide policy makers and implementers in reducing the dual burden of DM and TB. This was developed through a 2-year consultative process, with WHO giving clearance to develop a Framework rather than Guidelines due to lack of strong evidence to support some of the suggested interventions. The Framework was released in August 2011, and serves as a guide to help policy makers and implementers to move forward to combat the looming epidemic [25]. It will be important to ensure that interventions are delivered within the context of general health systems and take account of other chronic non-communicable diseases, and that engagement is sought both with and from civil society.

One of the important activities of the Collaborative Framework is the routine implementation of bi-directional screening of the two diseases [26]. The ways of screening, recording and reporting for

the two diseases in routine health care settings were not well determined, and these knowledge gaps needed to be addressed. [26, 27]

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