TUBERCULOSIS AND DIABETES MELLITUS- NOT A SWEET ASSOCIATION!

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ABSTRACT

BACKGROUND

Tuberculosis (TB) continues to be the leading killer among bacterial diseases worldwide. Diabetes is making people three times more susceptible to get active tuberculosis infection. Diabetes Mellitus (DM) is quietly fuelling the spread of tuberculosis. The association between diabetes and TB may be the next challenge for global tuberculosis control worldwide.

This study aims to find out proportion of DM among pulmonary tuberculosis patients and proportion of DM among patients with different sputum bacillary load.

MATERIALS AND METHODS

An observational cross-sectional study was conducted at MLN Medical College, Allahabad. A total of 1691 presumptive TB cases aged ≥ 18 years were enrolled, out of them 257 sputum smear positive pulmonary TB cases were included in the study. Data were collected using a structured questionnaire to elicit demographic and clinical variables including a history of diabetes. An HbA1c value of 6.5% or above was considered diagnostic of DM. Data was analysed on Microsoft Office Excel worksheet.

RESULTS

Out of total 1691 presumptive TB cases enrolled, 257 were diagnosed as sputum smear positive pulmonary TB cases. Both TB and DM were more common among males. Proportion of DM among sputum positive pulmonary TB patients was 7.39%. Proportion of DM is 8.33% among patients with bacillary load 3+ and 7.04% among patients with bacillary load 1+. Proportion of DM increases in pulmonary TB patients with older age. DM proportion was 3.7% among patients age < 40 years, while proportion was 14.2% among patients age > 60 years (p-value= 0.012).

CONCLUSION

In conclusion, this study shows a high proportion of DM among males, patients with active TB, older age group and in patients with high sputum bacillary load. An improved understanding of the bidirectional relationship of the two diseases is necessary for proper planning and collaboration to reduce the dual burden of diabetes and TB. We should increase public awareness about the risk factors or association of TB and DM together.

KEYWORDS

Tuberculosis, Diabetes Mellitus.

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BACKGROUND

Tuberculosis (TB) continues to be the leading killer among bacterial diseases worldwide. In 2015, there were an estimated 10.4 million new (incident) TB cases worldwide and 1.7 million people died from the disease.^[1] India accounts for around 27% of the world's TB cases.^[1]

Diabetes Mellitus (DM) is a chronic, non-communicable disease that weakens the immune system, making people with diabetes 3 times more likely to get active TB as compared to non-diabetics.^[2] Diabetes is no longer a disease of predominantly rich nations; its prevalence has been rising more rapidly in middle and low-income countries.^[3] The number of DM patients increased from 108 million in 1980 to

422 million 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.^[4]

Richard Morton in his Phthisiologia stated that TB and DM association has been known since Roman times.^[5] Susruta also described relation of TB and DM and Avicenna in his Canon of Medicine stated that 'phthisis' is often complicated by DM.^[6]

These two diseases are world's leading causes of death and disability. Diabetes mellitus is quietly fuelling the spread of tuberculosis. The association between diabetes and TB may be the next challenge for global tuberculosis control worldwide. A good planning, collaboration and implementation are necessary to reduce the dual burden of DM and TB. This study aims to find out proportion of DM among pulmonary tuberculosis patients and proportion of DM among patients with different sputum bacillary load.

MATERIALS AND METHODS

The present study comprised of patients attending the Department of Pulmonary Medicine, MLN Medical College, Allahabad, during the period from January 2017 to June 2017.

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Study Design

This was an observational cross-sectional study assessing proportion of Diabetes Mellitus among pulmonary tuberculosis cases.

Study Sample

Total 1691 patients (inpatients and outpatients) of presumptive TB cases attending Department of Pulmonary Medicine, MLN Medical College, Allahabad, were registered during the course of the study. Sputum smear microscopy is performed in all presumptive TB cases.

STUDY QUESTIONNAIRE Department of Pulmonary Medicine MLN Medical College, Allahabad	
Name of Patient _____	Age (in years) _____ Gender _____
Address of Patient _____	
Height (in cm) _____	Weight (in Kg) _____ BMI _____
Occupation _____	
Symptoms Suggestive of Tuberculosis: Cough ☐ , Expectoration ☐ , Evening rise of temperature ☐ , Fatigue ☐ , Night Sweat ☐ , Weight loss ☐ , Haemoptysis ☐ , Appetite loss ☐ Duration of illness - • Any previous history of Anti-tubercular drug intake: Yes ☐ No ☐ • History of contact with pulmonary tuberculosis patients: Yes ☐ No ☐ • Sputum Smear Grading by LED fluorescence microscopy (as per RNTCP) Negative ☐ 1+ ☐ 2+ ☐ 3+ ☐	
Symptoms suggestive of Diabetes: Increase thirst ☐ , Increase frequency of micturition ☐ , weight loss ☐ , Blurring of vision ☐ , lower extremity paresthesia ☐ • HbA1c - _____ • Previous history of Diabetes present: Yes ☐ No ☐ • Any family history of Diabetes: Yes ☐ No ☐ • History of any liver or kidney disease: Yes ☐ No ☐ • History of any psychiatric illness: Yes ☐ No ☐ • History of any immune-compromised state: Yes ☐ No ☐ • History of any immunosuppressive drug intake: Yes ☐ No ☐	
Date - _____	Signature of Investigator _____

Case Selection

All patients aged > 18 years of either sex with presumptive TB cases were enrolled in this study as per inclusion and exclusion criteria. Out of 1691 presumptive TB cases; 257 were diagnosed as sputum smear positive pulmonary TB cases and were included in the study.

Inclusion Criteria

1. Patients with sign and symptom suggestive of tuberculosis.

Exclusion Criteria

1. Patient not giving consent for participation in the study.
2. Pregnant women.
3. Patient with co-morbid illness like AIDS, liver disease and psychiatric illness.

Data Collection and Analysis

Data were collected using a structured questionnaire to elicit demographic and clinical variables including history of diabetes and analysed on Microsoft Office Excel worksheet. For patients consenting to DM screening, blood samples were collected and glycosylated haemoglobin (HbA1c) levels were measured from whole blood. An HbA1c value of 6.5% or above was considered diagnostic of DM, in line with

recommendations of American Diabetes Association.^[7] For patients with self-reported DM, a glycosylated haemoglobin (HbA1c) level 7% was taken to indicate poorly controlled disease.

Investigations

1. Routine haematological (Hb, TLC, DLC, ESR, GBP), liver function test and kidney function test.
2. HbA1c.
3. Bacteriological examination (sputum smear examination for M. tuberculosis by LED fluorescence microscope).
4. Chest radiograph postero-anterior view.

Sputum Smear Fluorescence Microscopy Grading (As per RNTCP)

Auramine O Fluorescent Staining Grading (Using 20 or 25x Objective and 10x Eye Piece)	Reporting /Grading
> 100 AFB/field after examination of 20 fields	Positive, 3+
11 - 100 AFB/field after examination of 50 fields	Positive, 2+
1 - 10 AFB/ field after examination of 100 fields	Positive, 1+

RESULTS

A total of 1691 presumptive TB cases were enrolled in this study, but only 257 were having sputum smear positive pulmonary tuberculosis. Out of 257 sputum smear positive patients, TB was more common among males (n= 179) than female (n= 78) and DM is also common among males (n= 15) than females (n= 4).

Proportion of DM among sputum positive pulmonary TB patients (7.39%) was significantly more than sputum negative suspects [Table 1].

Sputum AFB Smear Stain of Presumptive TB Cases (n= 1691)	DM	Non-DM
Positive (n= 257)	19 (7.39%)	238
Negative (n= 1434)	51 (3.55%)	1383

Table 1. Proportion of DM among Pulmonary Tuberculosis Patients

(P-value= 0.0095)

Although DM was found associated with greater bacillary load among sputum smear positive pulmonary tuberculosis patients, this difference was not statistically significant. Proportion of DM is 8.33% among patients with bacillary load 3+ and 7.04% among patients with bacillary load 1+ [Table 2].

Sputum Bacillary Load	DM	Non-DM
1+ (n= 142)	10 (7.04%)	132
2+ (n= 43)	3 (6.97%)	40
3+ (n= 72)	6 (8.33%)	66

Table 2. Proportion of DM among Patients with different Bacillary Load

(P-value= 0.93)

Among all sputum AFB smear positive pulmonary tuberculosis patients, proportion of DM is higher among patients with older age group. DM proportion was 3.7% among patients aged < 40 years, while proportion was 14.2% among patients aged > 60 years [Table 3].

Age Group	DM	Non-DM
18-40 years (n= 162)	6 (3.7%)	156
40-60 years (n= 67)	9 (13.4%)	58
> 60 years (n= 28)	4 (14.2%)	24

Table 3. Proportion of DM in different Age Group of Pulmonary TB Patients

(P-value= 0.012)

DISCUSSION

There are various factors which attribute for high association of diabetes with TB like low opsonic index, decreased bactericidal activity, decreased synthesis of collagen, impaired defensive function of reticuloendothelial cell, increased availability of glycerol in tissue that act as substrate for growth of Mycobacterium tuberculosis bacilli, lack of adequate substrate for antibody formation due to disturbed protein metabolism and lowered production of IL-1 beta and TNF alpha by peripheral blood monocytes.

Proportion of DM among Pulmonary Tuberculosis Patients

This study shows proportion of DM among pulmonary TB patients was 7.39%.

However, the prevalence of DM among TB patients ranged from 1.9% in Cotonou-Benin to 45% in Ebeye-Marshall Islands.^[8,9] Workneh MH et al systemic review shows an overall global median DM prevalence of 16% (IQR 9.0 - 25.3%).^[10]

Proportion of DM among Patients with different Bacillary Load

This study shows proportion of DM was higher among patients with high bacillary load. Matthew J Magee et al shows that patients with TB and DM were more likely to have a higher AFB smear grade (aOR 2.37, 95% CI 1.14 - 4.94).^[11]

Dooley, Kelly E et al shows higher sputum positivity in patients with DM.^[12]

Park SW et al shows a higher positive smear rates (p<0.001) among diabetics as compared with non-diabetics.^[13]

Proportion of DM in different Age Groups of Pulmonary TB Patients

This study shows that proportion of patients with DM is high among older age groups. Zheng C et al^[14] shows that median age of patients with TB-DM is 49.5 +- 11.8, p-value= 0.001. Wang Q et al^[15] also shows high proportion of DM as age increases.

CONCLUSION

In conclusion, this study shows a high proportion of DM among male patients with active TB, older age group and high sputum bacillary load. Diabetes mellitus is fuelling the spread of tuberculosis. So, an improved understanding of the bidirectional relationship of the two diseases is necessary for proper planning and collaboration to reduce the dual burden of diabetes and TB. We should increase public awareness about the risk factors or association of TB and DM together.

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