IMPACT OF DIABETES MELLITUS ON TREATMENT OUTCOME OF MULTIDRUG RESISTANT PULMONARY TUBERCULOSIS

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ABSTRACT

BACKGROUND

Multiple studies have indicated that patients of pulmonary tuberculosis with diabetes mellitus may experience poor outcome. Emergence of Multidrug Resistant-TB has further complicated the situation, as its management may be challenging in presence of diabetes. There is a paucity of data on effect of diabetes on outcome of MDR-TB in Indian context.

The study aimed to assess the effect of Diabetes Mellitus on mean time for sputum culture conversion and treatment outcome in patients of Multidrug Resistant Pulmonary Tuberculosis.

MATERIALS AND METHODS

The present observational cross-sectional study was conducted at Drug Resistant-TB centre, SRN Hospital, MLN Medical College, Allahabad. 144 diagnosed patients of MDR-TB were treated with Category IV DOTS and were retrospectively analysed for the effect of DM as a comorbidity on their outcome on treatment completion. The diagnosis of Diabetes Mellitus and treatment outcomes were defined as per WHO guidelines.

RESULTS

Out of 144 MDR-TB patients, 13 (9.03%) had co-existing Diabetes Mellitus. Patients having MDR-TB with Diabetes had longer sputum culture conversion time (131.4 ± 40.99 vs. 118.72 ± 41.54 days, $p = 0.358$) compared to MDR-TB patients without diabetes. They also had 2.75 times higher odds of death than patients in non-diabetic group (53.85% vs. 30.47%, 95% confidence interval [CI] 0.869 to 8.717). Non-diabetics had 1.84 times higher odds of culture negativity at 6 months (54.26% vs. 38.46%, CI=0.57 to 5.91) and 1.73 times odds of successful treatment (44.53% vs. 30.77%, CI= 0.51 to 5.91) compared to diabetic patients. 12.5% patients defaulted on treatment in non-diabetic group, while diabetic group had no default. 15.38% patients failed treatment in diabetic group compared to 12.5% in non-diabetic group ($p = 0.667$). Outcome of 3 patients was not known, since they were transferred out.

CONCLUSION

Diabetes Mellitus as a comorbidity was associated with longer culture conversion time, decreased success rate, higher treatment failure and higher death rate among patients of MDR-TB, but the results were not found to be statistically significant which may be due to small sample size in the MDR-TB with diabetes group.

KEY WORDS

MDR TB, Diabetes Mellitus, Pulmonary Tuberculosis, Sputum Conversion.

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BACKGROUND

Multiple studies have indicated that patients of pulmonary tuberculosis with diabetes mellitus (DM) may experience poor outcome. Emergence of Multidrug Resistant tuberculosis (MDR-TB) has further complicated the situation, as its management may be challenging in presence of diabetes. In the early 20th century the effect of DM on TB was of great concern to investigators, but this was neglected

in the second half of the 20th century with the emergence of proper treatment for both diabetes and pulmonary tuberculosis.^{1,2} The link of DM and TB is more prominent in developing countries, where TB is endemic and the prevalence of Diabetes is rising. In recent decades with the increasing prevalence of TB, particularly Multidrug-Resistant TB (MDR-TB) and DM cases in the world, the relationship is re-emerging as a significant public health problem.³

There is a paucity of data on effect of diabetes on outcome of MDR-TB in Indian context. Globally, in 2016 an estimated 4.1% of new cases and 19% of previously treated cases had MDR/ RR-TB. In 2016 there were 600,000 new cases with resistance to rifampicin (RRTB), the most effective first-line drug, of which 490,000 had multidrug-resistant TB (MDR-TB). Almost half (47%) of these cases were in India, China and the Russian Federation.⁴ Recently, along with the convergence of the diabetes mellitus (DM) and TB epidemics, the high prevalence of DM among MDR-TB

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patients is a serious cause for concern with a range of 10%-23% of MDR-TB patients having DM.⁵⁻⁸

Diabetes triples a person's risk of developing tuberculosis. About 15% of TB cases globally may be linked to diabetes. TB can temporarily cause impaired glucose tolerance, which is a risk factor for developing diabetes. About 422 million people worldwide were living with diabetes in 2014. In 2014, the global prevalence of diabetes was estimated to be 8.5% among adults aged 18+ years. In 2012, diabetes was the direct cause of 1.5 million deaths. WHO projects that diabetes will be the 7th leading cause of death in 2030. In 1980, diabetes prevalence was highest in high-income countries, now it is similar in both high- and low-income countries.⁹

Aims and Objectives

- To assess the effect of diabetes on mean time for sputum culture conversion in patients of MDR-TB.
- To assess the effect of diabetes on treatment outcome in patients of MDR-TB.

MATERIALS AND METHODS

This retrospective observational study of Drug-Resistant TB Centre was conducted in SRN Hospital, MLN Medical College, Allahabad, India. A total of 144 diagnosed patients of MDR-TB under Programmatic Management of Drug-Resistant Tuberculosis (PMDT), registered on Category-IV DOTS between March 2013 and January 2014 were retrospectively analysed for the effect of DM as a comorbidity on: - Mean sputum conversion time and treatment outcome on completion.

Inclusion Criteria

1. Diagnosed patients of MDR-TB under PMDT by CB-NAAT.
2. Aged above 20 years.

Exclusion Criteria

Patients were excluded from the study for any of the following conditions-

1. Pregnancy.
2. HIV infection.
3. Connective tissue disorders.
4. Chronic renal failure.
5. Chronic liver disease.
6. Malignancies on long-term steroid or cytotoxic drug therapy.
7. Chronic alcoholic.

Statistical Analysis

Chi-square test and independent 't' test were used for statistical analysis. 95% Confidence Interval of the parameters were also calculated. All statistical measurements were done using R version 3.1.2

RESULTS

Total number of patients enrolled in the study: 144. Out of 144 MDR-TB patients were 13 (9.03%), who had co-existing Diabetes Mellitus.

Characteristics	MDR-TB with DM	MDR-TB without DM	P-value
No. of Patients (%)	13 (9.03%)	131 (90.97%)	
Mean Age (In Years)	38.61 ± 12.11	30.83 ± 12.66	0.0357
Sex	12 M/ 1 F	96 M/ 35 F	
Mean Time for Culture Conversion (In Days)	131.4 ± 40.99	118.72 ± 41.54	0.358

Table 1. Comparison of Demographic and Clinical Characteristics in MDR-TB Patients with and without Diabetes Mellitus

Patients having MDR-TB with diabetes had longer sputum culture conversion time (131.4 ± 40.99 vs. 118.72 ± 41.54 days) as compared to patients without diabetes. On applying T-Test between these two groups, the p-value is 0.0357 which is statistically significant.

Outcome	MDR-TB with DM	MDR-TB without DM	Odds Ratio (95% Confidence Interval)	P-value
No. of patients who are culture negative at the end of 6 months (%)	5 (38.46%)	70 (54.26%)	1.835 (0.57-5.91)	0.31
Favourable outcome (Cured + Treatment completed)	4 (30.77%)	57 (44.53%)	1.733 (0.508-5.914)	0.38
Died during treatment	7 (53.85%)	39 (30.47%)	2.75 (0.869-8.7171)	0.08
Default	0	16 (12.5%)	0.259 (0.014-4.57)	0.356
Failure	2 (15.38%)	16 (12.5%)	1.307 (0.265-6.439)	0.742

Table 2. Comparison of Treatment Outcomes between MDR-TB Patients with and without Diabetes Mellitus

The odds of culture negativity at 6 months was 1.84 times higher in non-diabetic group as compared to diabetic group (54.26% vs. 38.46%, CI= 0.57 to 5.91). On applying T-Test between these two groups, the p-value is 0.31 which is statistically not significant.

The odds of successful treatment were 1.73 times higher in non-diabetic group compared to diabetic group (44.53% vs. 30.77%, CI= 0.51 to 5.91). On applying T-Test between these two groups, the p-value is 0.38 which is statistically not significant.

The odds of death in patients with diabetes was 2.75 times higher than patients without diabetes (53.85% vs. 30.47%, 95% CI= 0.869 to 8.717). On applying T-Test between these two groups, the p-value is 0.08 which is statistically not significant.

12.5% patients defaulted on treatment in non-diabetic group, while diabetic group had no defaults. On applying T-Test between these two groups, the p-value is 0.356 which is statistically not significant.

15.38% patients failed treatment in diabetic group compared to 12.5% in non-diabetic. On applying T-Test between these two groups, the p-value is 0.742 which is statistically not significant.

The number of patients who turned out to be XDR were 7.69% in diabetic group and 3.12% in non-diabetic group). On applying T-Test between these two groups, the p-value is 0.381 which is statistically not significant.

Outcome of 3 patients was not known since they were transferred out.

DISCUSSION

- The growing prevalence of TB-DM comorbidity worldwide has provided a new challenge to clinical management and health systems control strategy [34]. It was observed that patients who have DM complicated with TB often experience delayed sputum culture conversion, increased risk of death and recurrence.^{10,11-13}
- The reasons for a higher MDR rate in patients with TB-DM comorbidity are not thoroughly understood; however, they may differ by different MDR type (primary or secondary). The combination of impaired immune system in DM and bacterial genetics might be a reasonable explanation for primary MDR. It has been reported that poor glucose control is often associated with dysfunction of phagocytosis, reactive oxygen species (ROS) production, chemotaxis and T-cell reaction in DM patients.¹⁴
 - Earlier studies had shown that proportion of cases of MDR-TB was significantly higher in patients with coexisting diabetes; however, recent study showed no such association, but concomitant MDR-TB and DM may result in delayed sputum culture conversion and poor treatment outcomes as indicated by our study.¹⁵
 - Findings of our study were also supported by the study done by Young Ae Kang et al (2013), who also found diabetes to be a common comorbid condition among MDR-TB patients with a negative impact on treatment outcome. Also, in patients undergoing treatment for MDR-TB, DM was independently associated with an increased risk of both treatment failure and death.¹⁶

- Bashar et al reported an increased risk of MDR-TB and relapse with resistant strains among diabetic patients.¹⁵

CONCLUSION

- Diabetes as a comorbidity was associated with longer culture conversion time, decreased success rate, higher treatment failure and higher death rate among patients of MDR-TB.
- But in our study the results were not found to be statistically significant, which may be due to small sample size in the MDR-TB with diabetes group.

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