Diabetes Mellitus and the threat to Tuberculosis control-A study among new Sputum positive Tuberculosis patients

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Abstract
Background: Tuberculosis, a disease of great antiquity has become the most important communicable disease in the world. Diabetes Mellitus has been described as a risk factor for development, failure and relapse of Tuberculosis. Prevalence of Diabetes among follow up smear positives of newly diagnosed Tuberculosis patients were studied.

Methodology/Principal Findings: The study was conducted among 6 Tuberculosis units (TU) in the northern part of Kerala, India from January 2013 to June 2014. Screening of all Tuberculosis patients for Diabetes is being now routinely done under the RNTCP. Among the 1434 new smear positive patients during the time period, we identified 320 Follow up smear positives of which 85 (26.6%) were diabetic.

Conclusions/Significance: This study was done to identify Diabetes Mellitus as a comorbidity among follow up smear positives of newly diagnosed Pulmonary Tuberculosis patients. Early diagnosis with strict monitoring and optimisation of Diabetes among Tuberculosis patients would be mandatory to achieve cure, prevent relapse and reduce the development of Drug resistance.

Keywords: Pulmonary Tuberculosis, smear positive, Diabetes Mellitus.

Introduction
Tuberculosis,(TB) a disease of great antiquity has become the most important communicable disease in the world.In 2015, 10.4 million people fell ill with TB and 1.8 million died from the disease. Over 95% of TB deaths occur in low- and middle-income countries.¹ Diabetics have a higher risk of developing TB compared to non diabetics. About 10% of TB cases globally are linked to diabetes. Diabetes is associated with progression of latent TB to active TB, increased relapse after completion of treatment, failure of treatment and death.²,³ Kerala is also the Diabetic capital of India with an estimated community prevalence of 16–20% and is known to have a high prevalence of Diabetes in TB patients, with a recent study reporting a prevalence of 44%.⁴ We assessed a large cohort of new smear positive Pulmonary TB patients registered for first-line anti-TB treatment, whose follow up smears remained positive to determine Diabetes as a comorbidity. At present, there are limited studies in Kerala which have evaluated this.
Objectives
To assess the prevalence of diabetes mellitus among follow up smear positives in newly treated pulmonary tuberculosis patients.

Materials and Method
This was a cohort study conducted in all follow up smear positives among sputum positive pulmonary TB patients aged more than 6 years attending Tuberculosis Units in Kozhikode district, Kerala, India from January 1, 2013 to June 30, 2014 under the Revised National Tuberculosis Control Programme (RNTCP).

Study Procedure
All follow up positives among new smear positive Pulmonary Tuberculosis patients attending the Tuberculosis Units (TU) in Kozhikode from January 2013 onwards were identified from the respective TB registers in each of the 6 TUs. TB units (TU) are sub-district level tuberculosis programme management units covering a population of 500,000, which further cater to a number of peripheral health institutions. Follow up positives were defined as any patient with Pulmonary Tuberculosis who was smear positive at initiation of treatment and failed to convert to smear negative status or a patient, who initially smear converted, but became smear positive at any of the follow up smear examinations. After obtaining permission from the District Tuberculosis officer, the Medical Officer in charge of respective TUs and clearance from the Institutional Ethics committee, we collected data from the Tuberculosis registers available at the 6 tuberculosis units in Kozhikode using a pre structured questionnaire. The risk factor analysed was the presence of Diabetes Mellitus. Diabetes Mellitus was defined by a Fasting Blood sugar of 126mg/dL or a Random Blood sugar of 200mg/dL. Blood sugar values were available from the TB register in the particular TU.

Observations and Results
Among the 1434 new smear positive patients, we identified 320 Follow up positives. 150 patients belonged to an age distribution of 10-50 yrs and 170 people were >50 years. Majority of the patients belonged to the 51-80 age group (53.1%). None of the patients were immigrants and all were permanent residents of Kerala. Sex distribution of these 320 patients showed 269 males and 51 females. Analysis of the baseline (initial) smear status of patients showed that 263 of the 320 patients (82%) were either 2+ or 3+ as seen in Table 1.

Table 1- Sputum status at initiation of treatment

| Sputum status | Number(n=320) | Percentage |
|---------------|---------------|------------|
| 3+            | 182           | 56.9       |
| 2+            | 81            | 25.3       |
| 1+            | 51            | 15.9       |
| Scanty        | 6             | 1.9        |

85 of the 320 follow up patients (26.6%) were diabetic as seen in Table 2

Table 2 showing Diabetics among the follow up positives.

| Diabetes | Frequency | Percent |
|----------|-----------|---------|
| Present  | 85        | 26.6    |
| Absent   | 235       | 73.4    |
| Total    | 320       | 100.0   |

Discussion
In general, the bacillary population in smear-positive pulmonary TB is larger than in smear-negative pulmonary TB and extra-pulmonary TB and they are the source of transmission to the general public. We therefore specifically selected smear positive Pulmonary TB patients for our study. Among the 1434 new smear positive patients in our study, there were 320 follow up smear positives of which 85 (26.6%) were diabetic. The Diabetic population in our study was high with prevalence (26.6%) nearly two times that of the national data among TB patients. Persistent smear positivity did not indicate drug resistance and most likely indicates dead bacilli, delayed conversion because of higher bacterial loads as in cavities, the presence of comorbidities like Diabetes Mellitus, drug defaulting or rarely malabsorption.
People with diabetes have two -three times higher risk of TB compared to non diabetics. About 10% of TB cases globally are linked to diabetes. Diabetes mellitus is associated with progression of latent TB to active TB, increased relapse after completion of treatment, failure of treatment and death.\textsuperscript{5,6} Diabetes as a risk factor has been studied in many of the drug resistance surveys or studies. A cross sectional survey of TB patients registered in Kerala showed that among 552 TB patients, 44% had Diabetes Mellitus with 21% being newly diagnosed.\textsuperscript{4} Another study among peripheral health centres in a district in Kerala showed that there was high prevalence of undiagnosed diabetes among TB patients with a prevalence of 32%.\textsuperscript{7} In India a pilot project was implemented to assess feasibility and to know the prevalence of Diabetes mellitus among TB patients. Of 8269 TB patients, 1084(13%) were found to have Diabetes. 8% were previously diagnosed and 5% were new cases. They also found a higher prevalence among South Indians(20%) as compared to North Indians (10%) with statistical significance(p<0.001).\textsuperscript{8} A study conducted in South India assessing the outcome among new cases of Tuberculosis showed that poor glycemic control was associated with more severe forms of Pulmonary Tuberculosis as assessed bacteriologically and by Chest Radiographs.\textsuperscript{9}

**Conclusion**

This study was done to identify Diabetes Mellitus as a comorbidity among follow up smear positives of newly diagnosed Pulmonary Tuberculosis. We found that around 26.6% of the follow up positives had Diabetes Mellitus. Early diagnosis with strict monitoring and optimisation of Diabetes among Tuberculosis patients would be mandatory to achieve cure, prevent relapse and reduce the development of Drug resistance.

**Limitations of the study**

Study was mainly a record based study and therefore has its inherent limitations of record review studies. However, the RNTCP programme is supervised and monitored regularly from various staff and includes periodic data validation, hence the likelihood of any recording errors are minimal. Other co-morbidities like smoking, alcoholism, COPD, which could have also influenced the final outcome, were not studied.

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