Prevalence of Co morbidities among patients having Multi Drug Resistant Tuberculosis: A Retrospective Analysis

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Abstract
The comorbid conditions may have both impact as risk factor for developing MDR TB and they may influence the treatment outcomes as well. This study was planned with an objective of determining the prevalence of co morbid conditions associated with MDR-TB at the time of treatment initiation at Drug Resistant Tuberculosis Centre, Ajmer (Rajasthan), India. Data was extracted by reviewing of medical records of MDR-TB patients maintained at DR-TB centre retrospectively. Data of 127 patients were found eligible for study. There were 101 (79.5%) males and 26(20.4%) females with mean age of study group was 38.6 years (with C.I.(95%) of mean±2.27). Mean pre-treatment BMI was 15.81 Kg/m2 (C.I (95%) of mean was ±0.40). Among these 127 patients, comorbid conditions were present in 51 (40.1%) patients. Among patients with comorbidities, majority of patients had single comorbid illness (n=43, 84.3%) while 8 (15.6%) patients were having dual comorbidities. Among single comorbid states, COPD was found most common (n=16, 31.3%). In conclusion, great proportion of patient with MDR TB in our study were found to have comorbid conditions. Proper identifications and management of such concurrent medical conditions is vital as they may affect outcome of treatment which itself is challenging.

Keywords: MDR-TB, Comorbid conditions, Outcome.

Introduction
Multi drug resistant tuberculosis (MDR- TB) is a global public health threat. MDR TB is defined as resistance to at-least rifampicin and isoniazid[1]. The estimated incidence of tuberculosis (TB) cases were around 2800000 in India as reported by Global TB report 2017 which contributes approximately near quarter of worlds TB cases [2]. The same report, estimated MDR TB/RR incidence rates were around 147000 in India in 2016[2]. The first national drug resistance survey in India, found rates of MDR among newly diagnosed TB cases to be 2.84% while among previously treated TB cases to be 11.60%[2]. The treatment of MDR-TB is lengthy and complex in nature[1].

The effect of associated comorbid conditions on treatment of drug sensitive TB especially HIV, Diabetes Mellitus (DM) has been well known[3]. The associated comorbidities may be one of
factors for poor response to MDR TB treatment[3]. The association of MDR-TB outcomes and associated comorbidities are also not well described in literature[3]. The comorbid conditions may have both impact as risk factor for developing MDR TB and they may influence the treatment outcomes as well[3]. Therefore their association is of paramount importance in these patients.

This study was planned with an objective of determining the prevalence of co morbid conditions associated with MDR-TB at the time of treatment initiation at Drug Resistant Tuberculosis (DR-TB) Centre, Ajmer (Rajasthan), India.

Methodology

This was a hospital based cross sectional study conducted after approval from institutional ethical committee. All confirmed multidrug resistant pulmonary tuberculosis patients as per RNTCP criteria[1] admitted for pre-treatment evaluation to our DR-TB Centre over year 2012 were included. The pre-treatment evaluation consist of detailed clinical evaluation, complete blood counts, blood sugar, renal function tests, liver function test, TSH levels, urine examination, chest X-ray, height and weight measurements and pregnancy test (for women in child bearing age group) with voluntary HIV testing etc[1]. Baseline information including medical comorbid conditions, baseline haematological, biochemical investigations, socio demographic profile, previous TB treatment, drug resistance pattern etc. were extracted from records maintained at DR-TB Centre. Patients underwent detailed clinical evaluation with great emphasis on previous and current medical comorbid conditions during pre-treatment evaluation. Patients were encouraged for self-reporting of any concurrent medical illness. Once the patient had given any history regarding comorbid medical conditions, the relevant documents and investigations were reviewed thoroughly. Medical comorbid conditions were extracted by relevant documents and appropriate investigations consistent with their diagnosis. Further, any other medical comorbid condition diagnosed during detailed pre-treatment clinical evaluation and investigations at DR-TB centre was also included in this study. Records maintained at DR-TB centre were analysed critically and data were extracted retrospectively. Exclusion criteria of patients were those with incomplete records or workup and those patients who were transferred to some other unit.

Statistical Analysis

Data collected were entered in Microsoft excel 2010 worksheet in the form of master chart. Categorical variables were expressed in absolute numbers or percentages and continuous variables were expressed as mean±SD. The statistical analysis was performed using MaxStat Lite version (Version 3.60).

Result

A total of 127 patients constituted final study population after selection criteria. There were 101 (79.5%) males and 26(20.4%) females with mean age of study group was 38.6 years (with C.I.(95%) of mean±2.27). Mean pre-treatment BMI was 15.81 Kg/m2 (C.I (95%) of mean was ±0.40). Among these 127 patients, comorbid conditions were present in 51 (40.1%) patients. Among patients with comorbidities, majority of patients had single comorbid illness (n=43, 84.3%) while 8 (15.6%) patients were having dual comorbidities. Among single comorbid states, chronic obstructive pulmonary disease (COPD) was found most common (n=16, 31.3%). Occupational lung disease were seen in 14 (27.4%) patients followed by 3 each of hepatic and nervous system involvement. Diabetes & HIV association was found in 2 and 1 patients respectively. Among dual comorbid conditions, COPD with silicosis (n=3) was most common followed by Diabetes Mellitus with COPD (n=2). No comorbid conditions was found in 76 (59.8%) of patients (Table 1).
### Table 1 Comorbidities at treatment initiation among MDR-TB patients

| S.No | Co-morbidities | Total No. of Patients (n=127) | Percentage |
|------|----------------|-----------------------------|------------|
| **A. Single comorbidity** | | | |
| 1 | COPD | 16 | 12.5% |
| 2 | Occupational lung disease 1. Silicosis | 14 | 11.0% |
| 3 | Hepatic disease* | 3 | 2.3% |
| 4 | Neurological disease** | 3 | 2.3% |
| 5 | Diabetes Mellitus | 2 | 1.5% |
| 6 | HIV | 1 | 0.7% |
| 7 | Cardiovascular disease | 1 | 0.7% |
| 8 | Renal disease | 0 | 0% |
| 9 | Others*** | 3 | 2.3% |
| **B. Dual Comorbidity** | | | |
| 1 | COPD & Silicosis | 3 | 2.3% |
| 2 | Diabetes Mellitus & COPD | 2 | 1.5% |
| 3 | Diabetes Mellitus & Hypertension | 1 | 0.7% |
| 4 | COPD & Cor pulmonale | 1 | 0.7% |
| 5 | COPD & Hypertension | 1 | 0.7% |
| 6 | Others | 0 | 0% |
| 7 | Total | 51 | 40.1% |
| **C. Without any Comorbidities** | | | |
| | 76 | 59.8% |

*All were HbsAg positive.
**One patient was having peripheral neuropathy while two others were known cases of epilepsy.
***One patient each of Atopic dermatitis, Bronchial asthma, Allergic rhinitis.

### Discussion

Co-morbidities were present in 51 (40.1%) patients in our study. Most common comorbid condition found was COPD in 16 (12.5%) patients in our study. In study by Dhingra et al[4], 10 (37.0%), patients suffered from co-morbidities, the most common was Diabetes Mellitus. In their study, outcome was not affected by comorbid conditions[4]. Similarly in study by Yew et al[5], 23 (36.5%) patients suffered from co-morbidities.

In a study conducted by Joseph et al[6], 12 (31.5%) patients had Diabetes Mellitus and it was found that response of diabetic patients was equally good as those without diabetes. Diabetes is known as immunosuppressive condition. A recent systematic review also pointed out no clear association between diabetes and poor treatment outcomes[3]. The role of DM as risk factor for development of MDR TB is currently viewed as controversial issue[7].

In our study only one (0.7%) patient was seropositive for HIV and was on ART before MDR TB treatment initiation. In an Indian study[8], 3 (4.40%) were HIV positive, similarly in a Tanzanian study, 9 (14%) were found to be HIV positive at time of treatment initiation [9]. Recent systematic review has found increased relative risk of poor treatment outcomes in patients with HIV positive status[3]. There were 14 (11.0%) patients having occupational lung disease (silicosis) in our study. Silicosis is an important medical condition which is known for impaired macrophages functions and increased risk for tuberculosis[10].

In our study, hepatic disease was present in 3 (2.3%) and all were HbsAg positive. We could not found the effect of hepatic disease on treatment outcomes in MDR TB patients on literature search; however many drugs that are used in MDR-TB regimen are known to affect hepatic functions[1]. Among dual co-morbid conditions, silicosis with COPD (n=3, 2.3%) was most common, however; again data on dual comorbidities are lacking in literature.

### Conclusion

Great proportion of patient with MDR TB in our study were found to have comorbid conditions.
Timely identifications and management of such concurrent medical conditions is vital as they may affect outcome of treatment which itself is challenging.

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