Section: Respiratory Medicine

Original Research Article

STUDY OF CLINICO-MICROBIOLOGICAL PROFILE TREATMENT OUTCOMES AND FOLLOW UP OF PATIENTS WITH DRUG RESISTANT TUBERCULOSIS IN PUDUCHERRY

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ABSTRACT

Background: Tuberculosis is one of the most common causes of death in world. Drug resistance has become more common in previously treated patients, who were treated irregularly or with improper regimens and doses. Aim is to look the clinico-microbiological profile, treatment outcomes, and follow-up of patients registered for DRTB and IRL at Puducherry tuberculosis unit.

Materials and Methods: This study included 73 patients who were treated for drug-resistant tuberculosis at DRTB/IRL during 2014-2020. Their clinical condition, microbiological parameters, resistance pattern, laboratory profiles, and radiological results were taken. Patients with favourable and unfavourable outcomes were followed up using random sampling method and their current clinical findings, sputum smear status, and radiological data were recorded.

Results: 73 patients were included with mean age of 43.83±15.20 years. Treatment outcomes as 78.08% cured, from cured patients 16% were died during follow up period, 1.4 % completed treatment, 4.1% died before completing treatment, 4.1% were lost to follow up and 2.7% had treatment failure. Previous TB history exists in 79.45% and 20.55% newly diagnosed.

Conclusion: Treatment success occurred more than 3/4th of cases, which is higher than WHO of 75% success rate. 16% patients who died the follow up period of study, resulted an unfavourable outcome.

Keywords: DRTB, Clinico-microbiological profile, Treatment outcomes, WHO.

INTRODUCTION

Tuberculosis (TB) is one of most top ten causes of mortality globally, a main source of illness, and an infectious agent causing largest ranked more of HIV/AIDS. In 2019, near to 10 million diagnosed to have tuberculosis (TB) and 1.4 million died as a result of the disease.[1] Tuberculosis is caused by the bacillus Mycobacterium tuberculosis, which is transmitted through the air when persons with TB exhale bacteria, such as through coughing. Lungs is the main part to get affected (pulmonary tuberculosis), and can also disturb other areas of the body (extrapulmonary TB). A million 'missing' untreated or improperly diagnosed cases are also unnoticed each year.[2] Drug-resistant tuberculosis (DR-TB) has undermined TB control efforts and continues to cause significant morbidity and mortality in millions of people around the world. According to the World Health Organization,

approximately half a million new rifampicin-resistant tuberculosis infections were reported globally in 2019.[1] Mycobacterium tuberculosis that is multidrug-resistant (MDR) is isoniazid and rifampicin resistant and extensively drug-resistant (XDR) is rifampicin and isoniazid , at least one of the three injectable anti-TB medicines (capreomycin, kanamycin or amikacin) and any fluoroquinolone.[3] Due to difficulty of diagnosis, the long duration of treatment, the use of less effective and toxic medications, and lack of therapeutic choices, MDR-TB and XDR-TB treatment has been generally unsuccessful.[4,5,6] The current MDR-TB treatment success rate (the total number of people who have been cured and who have completed treatment) is extremely low.[7] According to a recent WHO global estimate, just 57% of MDR-TB patients were successfully treated in 2017.[1] Recent studies, on the other hand, have found that in some situations, treatment success rates are higher.[8,9,10,11] For example, 82.4% of MDR-TB patients in Taiwan8, 75.8% in Pakistan11, and 75.7% in Tanzania were successfully treated.[9] Poor MDR-TB treatment outcomes are linked to variety of heterogeneous and interconnected variables. MDR TB is recorded in 4.1 % of new TB cases worldwide. In line with previous surveys, the Indian government's First National Anti-Tuberculosis Drug Resistance Survey, conducted in collaboration with the World Health Organization (WHO) and the United States Agency for International Development (USAID), found that nearly 23% of new cases have drug resistance, with MDR-TB detected in 3% of cases.12 This study is being done, as there are no studies or data available to ascertain the prevalence and pattern of drug resistance tuberculosis in Puducherry region and also there is paucity of data on post treatment follow up of these patients.

MATERIALS AND METHODS

Objectives

a. To study the clinical profile of patients registered for Drug Resistant Tuberculosis treatment within Puducherry tuberculosis unit by review of treatment registry
b. To study the drug resistance pattern and the pattern of resistance mutation in these patients by review of Intermediate Reference lab (IRL) registry.
c. To study the treatment regimen, duration of treatment and treatment outcomes by review of treatment registry.
d. To correlate the clinical and microbiological profile with treatment outcomes in patient with Drug Resistant Tuberculosis within Puducherry tuberculosis unit.
e. To evaluate the symptomatology and radiological sequelae in patients available for clinical follow-up

Study design and settings

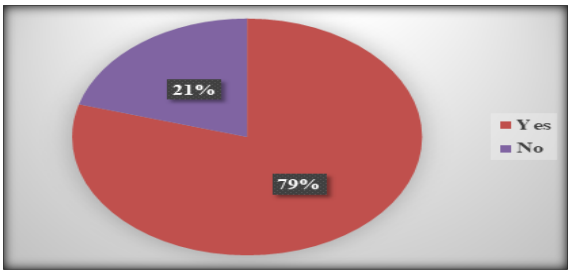
The present study was a retrospective register-based study and a follow up study. This study was conducted in a tertiary hospital in South India by the Department of Pulmonary Medicine. The study involved patients enrolled in IRL and DRTB registry. Drug resistance patients mentioned in inclusion criteria enrolled in Intermediate reference lab (IRL) from 2014-2019, and all patients with favourable (completed, cured, failure) and unfavourable outcomes were taken for this study. Patients who were enrolled for the treatment of drug-resistant TB at DRTB/IRL was selected by universal sampling method and their clinical status, microbiological parameters, drug resistance pattern, laboratory profiles and the radiological findings were noted. Patients with favourable and unfavourable outcomes (treatment completed, cured, failure, dead) were followed up based on random sampling method or a minimum sample size of 97 (as per sample size calculation). This study was planned to do on 97 however due to Covid 19 pandemic, the sample size was reduced to 73.

Those patients were followed up by house visits or by hospital visits and their current clinical findings, sputum smear status and radiological findings were noted and was compared with earlier. The results were analysed statistically and correlated with the clinical, microbiological and radiological findings. The data was entered with an excel sheet. Data was exported to Medcalc version 19.0 for further processing. All categorical variables were expressed as percentages and the continuous variables were expressed as mean ± standard deviation. All the patients above 18 years registered in IRL and DRTB and patient less than 18 years of age are excluded from the study.

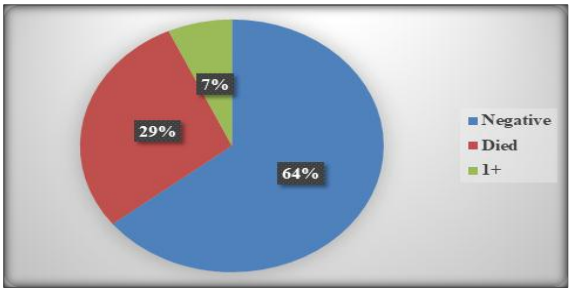
Sampling

- For the objectives a, b, c, d, the universal sampling was done.
- For the objective' e 'random sampling was done.

RESULTS



Graph 1: Distribution of subjects based on previous history



Graph 2: Distribution of subjects based on follow up sputum

The present study enrolled 73 patients with a mean age of 43.83±15.20 years and a median value of 45 years. This study population was male predominance (68.5%). The mean BMI was 22.44 kg/m2. The previous history of tuberculosis was existing in 79.45% of the study patients and remaining 20.55% did not had any previous history. The study showed that 76.71% of patients had mutation in both Rifampicin & Isoniazid and 23.29% of patients had mutation only in Rifampicin. (Graph-1). The present study observed the different patterns of mutations. Predominantly, the mutation was observed in RPO/ InhA/KatG genes (46.57%). 30.14% of patients had RPO/ InhA gene mutations and 23.3 % had only RPO gene mutations. 100 % of the patients were rifampicin resistant. 74% of patients were isoniazid INH resistant whereas, 26% of patients were sensitive. 1.37% of patients were resistant with ethambutol and remaining 91.8% was sensitive and 6.84% was unknown.95.9% of patients had sensitive with pyrazinamide. The sputum acid fast bacillus smear showed 50.68% as 1+, 34.2% as 2+ and 13.7% as 3+. The minimal number of patients showed negative. The initial chest x-ray revealed that 11% of the patients right UZ cavity. (Table-1) The shorter regimen was predominant in the present study (87.67%) and followed by oral drugs in longer regimen (6.8%). 78% of patients were cured completely and 2.7% were observed as treatment failure. 4.1% of patients were lost their follow-up and 1.4% was changed their treatment regimen. During the follow up study sputum AFB was done and showed 68.8 % negative for AFB and 6.8 % was showed 1+ and 28.8 % were died during the follow-up period. After treatment, during the follow up, the chest X-ray showed 19.2% were normal. 28.8% were died during the follow-up period. (Graph-2).

Table 1: Distribution of subjects based on pattern of mutation

Pattern of Mutation	Number	Percentage (%)
RPO/InhA/KatG	34	46.57
RPO/InhA	22	30.14
RPO	17	23.30
Total	73	100.0

DISCUSSION

Many countries have seen increased number of people newly diagnosed with TB since 2013. Globally India and Indonesia are the two countries which ranks first and second for estimated incident cases annually. Between 2013-2019 the notifications of newly diagnosed people with TB increases from 1.2 million to 2.2 million (+74%). In Indonesia, the number rose from 331703 in 2015 to 562 049 in 2019 (+69%). Even after increase in TB notifications, there had a large gap (2.9 million) between the numbers of people newly diagnosed and reported and in 2019, 10 million people estimated to have developed TB. This gap is due to a combination of underreporting of people diagnosed with TB and under diagnosis (if people with TB cannot access health care or are not diagnosed when they do). Five countries accounted for more than half of the global gap: India (17%), Nigeria (11%), Indonesia (10%), Pakistan (8%) and the Philippines (7%). In these countries especially, intensified efforts are required to reduce underreporting and improve access to diagnosis and treatment.[1]

There was some progress in testing, detection and treatment of MDR/RR-TB between 2018 and 2019. 2019 globally, TB patients who was bacteriologically confirmed people were tested for rifampicin resistance was 61%, up from 51% in 2017 and 7% in 2012. The similar findings were observed in the present study also. Coverage of testing was 59% for new and 81% for previously treated TB patients. A global total of 206 030 people with MDR/RR-TB were detected and notified in 2019, a 10% increase from 186 883 in 2018, and 177 099 people were enrolled in treatment, up from 156 205 in 2018.[1]

Even after these improvements, the people enrolled in treatment in 2019 was equivalent to 38% from the estimated number of people who were developed MDR/ RR-TB. In order to reduce this wide gap there requires some of the following like improving detection, increasing bacteriological confirmation among those diagnosed, expanding the coverage of testing for drug resistance for those who were bacteriologically confirmed and ensuring that all those diagnosed with MDR/RR-TB are enrolled in treatment. Our study, 73% of MDR-TB patients had a successful outcome and the treatment outcomes overall for the population were consistent with previously reported outcomes. A systematic review of 26 trials with a total of 4,959 MDR-TB patients were done was showing 62% of them met the definition of successful treatment.[1415] The 78% treatment success rate for our population was higher compared with the rate of 54% reported worldwide by WHO1 but less than the 86% achieved by

individualized MDR-TB treatment in the study by Bolhuis, et al,[16] In our study, 4.1% of patients were lost to follow-up and 1.4% of these re-initiated their treatment until completion. A global rate for loss to follow-up of 15%1 which was higher than the present study report as reported by WHO. The direct indicators of bacteriological load were sputum smears and cultures. The patient's infectious status, and ultimately, the success of treatment. For labelling the patient as non-infectious Conversion of initial sputum culture for the first three months is essential, this is an important indicator to determine whether or not it is necessary to extend the time of treatment.[17] In our study most patients with a successful outcome (78%) had a sputum culture negative conversion at two months while 22% of those with a poorer outcome had negative cultures in the same period. This is consistent with studies in which sputum culture conversion within two months was considered as a marker of a successful outcome in HIV negative patients.[13] In our study, smoking habits were associated with poor treatment outcomes. These results are in accordance with the results of the study of Tachfouti et al,[18] and a study conducted by Albuquerque et al,[19] they evaluated the association of smoking and unsuccessful treatment outcomes among TB patients. Another study by Bastos et al. reported that treatment success was more likely in non-smokers patients.[20] Smoking has been found to be associated with both relapse of TB and TB mortality.[21]

Limitations of the study

This is a record-based study, the actual evidence in study was only available from DRTB registry, IRL Lab Puducherry another is the practical difficulty in follow-up of patient because of covid pandemics and Limited number of subjects was another drawback.

CONCLUSION

The previous history of tuberculosis was existing in 79.45% and 20.55% newly diagnosed MDR-TB.76.71% of patient's had mutation of Rifampicin and Isoniazid. Majority of patients had mutations in RPO/InhA/KatG genes. All the patients were rifampicin-resistant whereas 74% was along with Isoniazid (INH) resistant. The shorter oral regimen was predominant and 78% of patients cured completely.

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