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A STUDY ON ASSESSMENT OF MULTIPLE DRUG RESISTANCE TUBERCULOSIS CASES IN ERODE DISTRICT UNDER RNTCP AND ITS PROPOSED CLINICAL PHARMACIST INTERVENTIONS

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ABSTRACT

The aim of our study is to assess the MDR TB cases in Erode district under RNTCP and to provide guidelines to the hospital administration regarding Tb and to evaluate the risk factors associated with Tb and provide proper counselling to the patients to reduce the impact of Tb among them. **Methods:** A bidirectional study on MDR Tb cases was conducted during the period of February 2016 – July 2016 at Government Head Quarters hospital under RNTCP in Erode district. **Results:** In our study, we collected 65 cases of MDR TB and it indicated that male (55.38%) patients were having more drug resistance as compared to female (44.61%)patients. We also concluded that smoking, alcohol consumption, diabetes, HIV is the major risk factors associated with the cause of emergence of Tb. **Conclusion:** Tuberculosis remains a worldwide public health problem which cannot be eradicated completely without proper adherence. HIV, cigarette smoking, alcoholism, diabetes, and poor adherence are major factors for development of MDR TB. In order to prevent the emergence of MDR TB, we must give patient information's regarding the importance of treatment adherence. Apart from that accurate susceptibility testing is necessary to identify the MDR TB cases.

KEYWORDS: Tuberculosis, Multiple Drug Resistance, Drug susceptibility testing, Centrifugation Based Nucleic Acid Amplification Assay.

INTRODUCTION

Tuberculosis is an infectious disease that is caused by the microorganism named mycobacterium tuberculosis and tubercle bacilli. This is a type of disease that is spread from person to person through air. TB usually affects the lungs, but it can also affect other parts of the, body such as brain, kidneys, or spine. Tuberculosis continues to dominate among infectious diseases globally due to its extreme contagious nature.[1]

Emergence of drug resistance in Tuberculosis is associated with a variety of management factors such as

- Health providers and other patient related factors, including deficient TB control programmes resulting in adequate administration of effective treatment.
- Poor case handling and inadequate or irregular drug supply
- Poor patient adherence or non- adherence to the patients to the prescribed drugs
- The epidemic of HIV infection
- Interruption of chemotherapy due to side effects[2]

MDR-TB

MDR-TB is defined as tuberculosis caused by a strain of Mycobacterium tuberculosis that grows, in vitro, in the presence of one or more anti-mycobacterial drugs.[3]

Spontaneous mutations lead to development of resistance randomly in large populations of M. Tuberculosis at a rate per cell division of 10^{-10} for Rifampin (RIF), 10^{-8} for Isoniazid (INH) and streptomycin, 10^{-6} to 10^{-8} for Fluoroquinolones, 10^{-7} for Ethambutol and 10^{-3} for Pyrazinamide.[4-5]

In the new cases of TB, nearly 5% were diagnosed as multidrug resistant (MDR) that is resistant to isoniazid and rifampicin, the two most effective anti-TB agents, which indicate an increase of 12% since 2004. [6] An additional 1 to 1.5 million prevalent cases of MDR-TB were estimated in 2006, resulting in as many as 2 million people with active disease. [7] For the successful treatment of MDR-TB requires the use of second-line TB drugs which is comparatively less effective.

Management of MDR-TB

The major challenge of scaling up MDR-TB treatment programs were the process of building laboratory capacity. Although DOTS requires only smear microscopy, MDR-TB treatment demands culture and DST capacity for the following: individual regimen design, regional surveillance to guide standardized regimen composition, and treatment monitoring. So implementation of a laboratory network for efficient transmission of samples and results between laboratories and clinical settings is vital.[8]

There exists a No. of programmatic approaches for managing MDR-TB management, with variability in the following elements: When to screen and treat, whether to use empirical therapy prior to laboratory confirmation of MDR-TB, how to individualize the regimen, how to monitor treatment response and where to deliver care.[9-10]

Drug Resistance

Individuals with latent tuberculosis infection will not have the active disease and it cannot be transmitted to others. However, reactivation of disease may occur if the host's immune systems are impaired.

- **Drug resistant tuberculosis** is the resistance to first line anti tubercular drug, either isoniazid or rifampicin.
- **Multi drug resistant tuberculosis** is resistance to isoniazid and rifampicin and possibly additional agents.
- **Extensively drug resistant tuberculosis** is resistance to Isoniazid, Rifampicin, Fluoroquinolones[3]

Study Design

A bidirectional study on MDR Tb cases under a sample size of 65 patients was conducted during the period of February 2016 – July 2016 at Government Head Quarters hospital under RNTCP in Erode district.

Inclusion Criteria

The study population comprised of pulmonary and extra pulmonary patients whose ages are in between 15-80years, registered during the period of Feb 2016 to July 2016 in Government Headquarters Hospital, Erode.

Exclusion Criteria

Patients who are not having MDR-TB cases are excluded.

Method of Data Collection

During our study, we reviewed the case sheets of all patients who met the inclusion criteria. Data was collected using a well-structured data collection proforma which includes patient's demographics, patient's case history, medication chart, culture reports and laboratory parameters. The laboratory parameters were reviewed regularly to check any deviations. The culture reports were also analyzed side by side.

Data Analysis

The data was analyzed using Graph pad version 5.03. Chi square test, Student T test, and percentage analysis were used to analyze the MDR TB and to monitor the treatment follow up. A p-value of ≤0.05 was considered to be significant. Using this value, the significance of results was calculated.

RESULTS

Distribution of Drug Resistance Based On Patients Demographics

Table 1: Out of 65 cases collected 55.38% of patients with MDR TB were males and 44.61% were females. In age wise categorization 44.61% of patients belonged to the age group of 36-50.

Based on Gender			
	Rifampicin (%)	**Rifampicin + INH (%)**	**Percentage (%)**
Male	47.69	7.69	55.38
Female	35.38	9.23	44.61
Based on Age Group (In yrs.)			
20-35	10.76	9.23	19.99
36 -50	23.07	21.53	44.61
51 – 65	21.53	12.30	33.83
> 65	0	1.53	1.53
Based on Year			
2014	7.69	9.23	16.92
2015	27.69	12.30	39.99
2016	20	23.07	43.07

Distribution of Drug Resistance Based On Site of Infection, Type and Treatment Outcome

Table 2: Based on site of infection, 98.48% of MDR were pulmonary TB. On analyzing various types of TB cases i.e., newly diagnosed, TB Relapse, and Default TB (Treatment Failure) it was evident that more percentage of MDR TB were reported in Default TB cases.

Based on site of infection			
	Rifampicin	**Rifampicin + INH**	**Percentage (%)**
Pulmonary TB	53.84	44.61	98.46
Extra pulmonary TB	1.53	0	1.53
Based on type of TB			
New	13.84	4.61	18.46
Relapse	7.69	15.38	23.07
Default	33.84	24.61	58.46
Based on Treatment Outcome (In %)			
Improved	21.53	29.23	50.76
Relapse	0	1.53	1.53
Default	15.38	0	15.38
Against Medical Advice	9.23	12.30	21.53
Death	10.76	9.23	19.99

Risk Factors

Table 3: Risk factors for the development of MDR TB were analyzed, i.e. patient with and without alcohol abuse, smoking, diabetes and HIV.

	Rifampicin	**Rifampicin + INH**	**Percentage (%)**
Alcohol Abuse			
Yes	12.30	4.61	16.91
No	43.07	40	83.07
Smoking Status			
Yes	43.07	32.30	75.37
No	12.30	12.30	24.60
Dizabetic Status			
Yes	3.07	4.61	7.692
No	52.30	40	92.30
HIV Status			
Yes	9.23	6.15	15.38
No	46.15	38.46	84.61

Distribution of Mdr Suspect Criteria and Resistant Drug

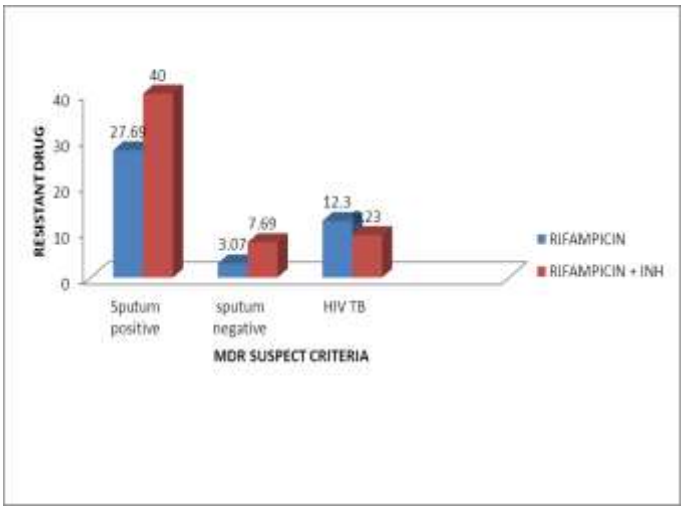

Fig 1: Based on the MDR Suspect Criteria, MDR TB was mostly found in sputum positive cases compared to sputum negative and HIV Tb cases.

DISCUSSION

In this bidirectional study, 65 MDR TB cases were analyzed in erode district under RNTCP. There are several cases in India and worldwide and this study adds to existing knowledge on Multi drug pattern on TB.

Out of 65 cases of MDR TB collected male (55.38%) patients contributed a greater proportion of drug resistance as compared to female (44.61%) patients. A similar study conducted by Muhammad Khurramet al., [11] in 2010 concluded that Pulmonary MDR-TB is common young males, in poverty related circumstances, and has poor outcome.

On survey of MDR TB cases from the year of 2014-2016, it showed that more drug resistance was increasing each year ie from 2014 to 2016.The distribution of drug resistance in various groups the 36-50 (44.61%) age group patients were having more drug resistance as compared to other groups followed by 51-65(33.84%) year.

HIV status is a risk factor for the development of MDR TB. We inferred from our study that out of 65 patients 10 were having HIV (15.38%) and in non HIV patients it was (84.61%). A reasonable study done by Susan van den Hof, *et al.*,[12] in 2015 concluded that recent meta analyses have indicated that, on average, new HIV-positive tuberculosis patients (TB) are at increased risk of multidrug -resistant (MDR)-TB compared with HIV-negative patients.

On studying the relation between MDR TB and alcohol consumption we came to a conclusion that alcohol abuse is a risk factor for developing MDR TB. Out of 65 cases collected 11 among them were alcohol abusers (16.92%). A comparative study done by A.C. Miller[13] suggests those individuals who drink alcohol should receive aggressive attention to optimize treatment adherence in order to minimize development of MDR TB.

Smoking status is a major risk factor for the emergence of multidrug resistant TB. In our study out of 65(75.38%) patients 49(24.61%) were smokers. A proportional study done by Pinar Parzali*et al.*[14] drawn a similar conclusion that smoking plays a vital role in the expansion of MDR TB.

Diabetes Mellitus is also a risk factor for developing Multi Drug Resistance in TB patients. In our study out of 65 patients, 5 (7.692%) were found to be diabetic. A relative study was conducted by Parvanesh Baghaei *et al.*,[15] in 2014 and concluded the same by a case control study with sample size 90 out of which 45 were diabetic and other 45 were non diabetic.

When we studied about the incidence of MDR TB in both Pulmonary (98.46%) and extra pulmonary (1.538%) tuberculosis we found that it was more prevalent in pulmonary TB patients as compared to extra pulmonary patients.

MDR TB was mostly diagnosed in default (58.46%) TB cases as compared to new (18.46%) TB and relapse.

Another conclusion drawn from the study was that, positive treatment outcomes were seen in both Rifampicin and isoniazid resistance patients (29.23%).

Based on the MDR Suspect Criteria, MDR TB was mostly found in sputum positive (67.69%) cases compared to sputum negative (10.76) and HIV Tb (21.53) cases.

CONCLUSION

Tuberculosis remains a worldwide public health problem which cannot be completely eradicated completely without proper adherence. From our study itself we could see that the resistance is increasing every year. Lack of adherence to treatment contributes to the incidence of MDR TB. In multi-drug resistance TB the patient won't respond to even isoniazid and rifampicin, the most powerful TB drugs.[16]

There are various reasons for the development of MDR TB including inadequate treatment. This can be due to number of factors like poor adherence or use of sub-standard drugs. Another reason is that MDR TB may get directly transmitted from one person to another.

It was evident that HIV, cigarette smoking, alcoholism, diabetes, and poor adherence are major factors for development of MDR TB. In order to prevent the emergence of MDR TB, patients must be aware about importance of treatment adherence.[17]

Apart from that, accurate susceptibility testing is necessary to identify the MDR TB cases and by having this conversion of MDR cases into XDR cases can be prevented.

ABBREVIATIONS

TB – Tuberculosis.

MDR – Multiple Drug Resistance.

RNTCP – Revised National Tuberculosis Control Program.

HIV – Human Immunodeficiency Virus.

DOTS – Directly Observed Treatment Short Course.

XDR – Extensively Drug Resistance Tuberculosis.

DST – Drug Susceptibility Testing.

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