

# TREATMENT OUTCOME OF MULTI-DRUG RESISTANT TUBERCULOSIS (MDR-TB).

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## ABSTRACT

**OBJECTIVE:** To assess the treatment outcome of multi-drug resistant tuberculosis (MDR-TB).

**PLACE AND DURATION:** People's University and Medical Health Sciences, Nawabshah during the period of four years from January 2007 to December 2010.

**MATERIAL AND METHOD:** Patients were selected from Pulmonology outpatient department and ward, after having confirmed MDR-TB by Laboratory AFB culture and DST (Drug Sensitivity Test). Patients were admitted in Pulmonology ward till sputum conversion was achieved. The details of demographic data, chemotherapy, adverse reactions to drugs, follow-up assessment as well as regular sputum bacteriology and chest radiograph result were recorded.

Medical records were reviewed of patients treated for MDR-TB from January 2007 to 2010 and monitored three years after initiation of treatment. Initial treatment outcomes and survival rates were analyzed.

**RESULTS:** 14 out of 36 patients (38.44%) treatment success rate was found at the end of treatment and 8 patients (22.24%) were failed to achieved sputum conversion by smear and culture at the end of MDR-TB treatment. Where as eight patients (22.24%) were defaulter and 4 patients (11.22%) were died and 2 patients (5.56%) were relapsed after completing their treatment.

**CONCLUSION:** Adequate TB control polices should be implemented to prevent the further spread of drug resistance.

**KEY WORDS:** MDR-TB, XDR-TB, AFB Sputum Smear, AFB Culture, Treatment Failure, DST.

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## INTRODUCTION

Multi-drug resistant tuberculosis is a growing hazard to human health worldwide and a threat to tuberculosis control, the management of MDR-TB is difficult, more expensive challenging and quite often leads to treatment failure.<sup>1</sup> Drug resistance is the end result of poor TB control, drug resistant form of tuberculosis is poised to kill tens of millions people across the world.<sup>2</sup>

MDR-TB is an iatrogenic problem (Man made error). MDR-TB is one of the earth's deadliest infection with resistant strain of mycobacterium tuberculosis. MDR-TB is defined as resistance to Rifampicin and Isoniazid with or without resistance to other anti-tuberculosis drug.<sup>3</sup> Increased prevalence of MDR-TB is due to incorrect regimens and poor patient's adherence.<sup>4</sup> Pakistan is one of the most adversely affected country

by MDR-TB it is caused by incorrect prescription, poor compliance, poor drug quality, irregular drug supply, inadequate TB control program, lack of DOTS results in MDR-TB. MDR-TB is more difficult and more expensive to treat; treatment of this disease can take up to 24 months with a combination of toxic, less potent drugs.

According to a recent W.H.O report, approximately 490,000 MDR-TB cases occur globally every year, corresponding to approximately 4.8% of the world's TB cases. MDR-TB is an increasing health problem in Pakistan. W.H.O report 2008 Geneva, the estimated cases of MDR-TB in Pakistan are 3.4% and 36% in new and previously treated cases of tuberculosis respectively. Globally Pakistan is ranked 8<sup>th</sup> in terms of estimated number of tuberculosis (TB) cases with an incidence of 181/100,000 persons.<sup>5</sup> Patients infected with MDR strains are not only difficult to cure but also more likely to remain sources of infection for a longer period of

time than those drug susceptible organism.<sup>6</sup> Uprising problem of treatment failure in pulmonary tuberculosis cases needs to find out the treatment outcome of MDR-TB patients with second line anti-tuberculosis drugs, whether the MDR-TB patients are treatable or not with second line anti-TB drugs.

XDR-TB is the occurrence of TB in person whose M. Tuberculosis isolates are resistance to Isoniazid and Rifampin Plus resistant to any Fluoroquinolone and at least one of three Kanamycin, Amikacin or Capreomycin. XDR is an extremely serious, emerging threat to public health and TB control. XDR-TB (Extensively Drug Resistant Tuberculosis) which cannot be cure by either first line or second line drugs.<sup>7</sup>

### MATERIAL AND METHODS

#### PLACE OF STUDY:

This prospective study was conducted on thirty six MDR-TB patients between January 2007 to 2010 at People's University of Medical & Health Sciences Nawabshah.

#### SELECTION OF PATIENTS:

Patients were selected from out patients department and Pulmonology ward after having confirmed MDR-TB by Laboratory identification and susceptibility test were enrolled.

#### INCLUSION CRITERIA:

Adult patients of TB with sputum for AFB culture and sensitivity report showing resistant to at least Rifampicin and Isoniazid.

#### EXCLUSION CRITERIA:

**Pregnancy, Mental illness.**

All Patients who were included in this study were admitted and treated with ofloxacin and at least three other second line anti-tuberculosis drugs based on drug susceptibility test. Patients were admitted in TB Ward till sputum conversion was achieved. Radiological examination was done by serial chest x-rays at least once every three months. Radiological severity was estimated by using the recommendation of the National Tuberculosis Association of the United States.<sup>8</sup> We used the modified six treatment outcome categories recommended by WHO (Cure, Default Death, Treatment Failure, Relapse and transfer out).<sup>9</sup>

Guidelines for the Programmatic Management of Drug- Resistant Tuberculosis, Geneva, Switzerland Publication No: WHO/HTM/TB/2006. 361. The duration of adequate treatment was defined as 18 months or more and 12 months or more after culture conversion.

Treatment was given daily and directly observed during the intensive phase (3-5 months) patients were closely observed for any side effects of second line drugs. During this period bacteriological monitoring was done by smear and culture monthly for 6 month then quarterly till the end of treatment (18-24 months). LFT, Urea, creatinine were also done at a monthly interval.

#### DEFINITION OF TREATMENT OUTCOME

**Cured:** A patient who has completed treatment for at least for 18 months and has been culture negative for the final 12 consecutive months of treatment.

**Death:** A patient who dies during the course of treatment.

**Failure:** A patient who remains culture positive at least 6 months or those who become consistently positive subsequently during treatment and require change treatment.

**Default:** A patient who had interrupted treatment for two or more consecutive months.

**Relapse:** A patient previously treated for TB or treatment completed and is diagnosed with bacteriological positive (smear or culture) tuberculosis.

### RESULTS

Demographic data of MDR-TB patients are presented in Table- 1

There were twenty three (63.88%) males and thirteen (36.12%) females with mean age of  $37.42 \pm 7.72$  years (Range 16-75 years) and mean weight  $40.65 \pm 7.70$  kg (Range 25-58 kg) nine (25%) out of thirty six patients were smoker and all of them were males. All the patients were having a definite history of anti-tuberculosis therapy varying from 5 months to 3 years. In this study all patients were acquired drug resistance MDR-TB.

Associated medical problem were seen in four patients, two of them had diabetes mellitus where as one was hypertensive and other one had pericardial effusion.

Resistant pattern of MDR-TB listed in Table-2.

Two drugs resistance were found in two patients (5.56%), three drugs seen in ten patients (27.78%), four drugs resistance were seen in ten patients (27.78%), five drugs resistance were found in ten patients (27.78%) and six drugs seen in four patients (11.12%) and remaining four patients were resistance to six drugs.

Table 1: Demographic Data of MDR-TB

Patients Characteristics	Number of Cases (n=36)	Percentage
Age		
Mean	37.42 + 7.72	
Range	(16-75 years)	
Sex		
Male	23	63.88 %
Female	13	36.12 %
Body weight (Kg)	40.65 + 7.70	
Smoker	9	25 %
History of contact with TB Patients	27	75 %
Previous History	5 month to 3 years	

Table 2:

Resistance to	Drugs	No. of Patients n=36	Total percent of Patients n=36
Two drugs	RH	2	2 (5.56%)
Three drugs	RHZ	3	10 (27.78%)
	RHE	3	
	RHS	4	
Four drugs	RHEZ	4	10 (27.78%)
	SRHE	6	
Five drugs	SREHZ	6	10 (27.78%)
	KSRH OFX	4	
Six drugs	KSRH OFX Z	2	4 (11.12%)
	KSRH OFX ETO	2	

R= Rifampcin,  
Z= Pyrazinamide,

H= Isoniazid,  
ETO= Ethionamide,

E= Ethambutol,  
OFX=Ofloxacin.

S=Streptomycin, K= Kanamycin,

Table 3: Outcomes of MDR-TB n=36

	Cure	Treatment Failure	Default	Died	Relapse
MDR-TB	14 (38.89%)	8 (22.24%)	6 (16.68%)	2 (5.56%)	2 (5.56%)
XDR-TB	-	-	2 (5.56%)	2 (5.56%)	-

28 patients (77.8%) out of 36 sputum smear and conversion rate was found, where as 8 (22.2%) patients were failed to achieved sputum smear and culture at the end of 5 months therapy. (P-value= 0.001, Chi Square = 44.44).

Finally the treatment outcome after two year of anti-tuberculosis treatment for MDR-TB was obtained in 36 patients, cure rate favourable clinical and bacteriological response was recorded in 14 (38.4%) out of 36 patients and treatment failure was found in 8 patients (22.24%) where as 8 patients (22.24%) defaulted and

treatment restarted, after 2 months they lost to follow up and failed to keep their OPD appointment, and 4 patients (11.12%) defaulted and 4 patients (11.12%) died before treatment completion and 2 patients (5.56%) were relapsed after completing their treatment.

## DISCUSSION

MDR-TB has a high mortality rate even with treatment. Treatment of MDR-TB is both difficult and expensive even in industrialized countries. The treatment success rate in this study was 38.89% (14/36) LOCK-

MAN reported cure rate (defined as completed > 6 months of therapy and had negative AFB smear result at the end of treatment of 37% (17/46), which is compatible to our study.<sup>10</sup> Default rate 22.24% (8/36) was high in our study. Authors have reported high default rates 28.9%.<sup>11, 12</sup> In resource limited countries, where default during treatment is high. We believe that the reason for default in our study was because of side effects of second line drugs and economic constraint i.e poverty. It has been reported patients who received initial therapy in Hospital had significantly higher treatment completion rate (79%) than those treated as out-patient alone (48%). Our treatment completion rate was low in spite of all patients being admitted in the initial phase. The relapse rate is quite low in this study. This could be because of the patients who benefitted from their own purchased good quality drugs. Relapse rate during the study period 2 patients (5.6%) reported with positive sputum among those who were successfully completed the treatment. The gap between completion of treatment and relapse was between 4-6 months (attempts were made to contact but failed to traced them) due to non availability of facilities for follow up.

The limitation of this study was that the patients were followed up with sputum smear and chest X-ray only as the facility for AFB culture on a large scale was not possible. The other limitation was lack of follow up after completion of treatment.

## CONCLUSION:

MDR-TB is a treatable disease with proper management and strategy. Adequate TB polices should be implemented to prevent the further development and spread of drug resistance.

## RECOMMENDATION

The top priority is not the management, but the prevention of MDR-TB by implementation of good National TB Program (NTP) using short course chemotherapy (SCC) by directly observed treatment short course (DOTS).

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