

OUTCOME OF COMMUNITY BASED THERAPY OF MULTI DRUG RESISTANT TUBERCULOSIS PATIENTS TREATED IN A TERTIARY CARE HOSPITAL OF KHYBER PAKHTUNKHWA

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ABSTRACT

OBJECTIVES: The objective of this study was to determine the treatment outcome of MDR-TB patients in a tertiary care hospital that acts as provincial reference point for MDR TB in Khyber Pakhtunkhwa province of Pakistan

SETTING: All cases of MDR-TB registered at Lady Reading Hospital Peshawar from October 2008 to December 2011 prior to the implementation of a formal Programmatic Management of Drug Resistant TB (PMDT) by National TB Control Programme (NTP).

METHODOLOGY: It was a cross sectional study to find out the outcome of MDR TB patients who received ambulatory community based treatment. Patients were provided with free drugs only and no other social or travel support was available due to lack of resources. Smear microscopy was available free of cost whereas sputum culture sensitivity was not. No tools for strict supervision and ensuring compliance were available except for a volunteer treatment supporter and contact by mobile phones.

RESULTS: 341 MDR-TB patients were registered during the period of the study out of which 145 (42.8%) were male and 196 (56.2%) were females. 221(64.8%) patients were between 9 - 30 years, 113 (33.1%) were between 31-60 years and 7 (2.1%) patients were above 61 years of age. The treatment outcome of the registered patients was that 134 (39.3%) patients completed their treatment, 80(23.5%) were cured, 70 (20.5%) died during the treatment, 50(14.7%) defaulted and 7(2.1%) were transferred out during the treatment.

CONCLUSION: Community based outpatient treatment of multidrug-resistant tuberculosis can be an effective strategy. High default rate of 14.5 % suggests that MDR TB requires a strong system for treatment supervision. Compliance with therapy can't be sustained if the supervision mechanisms are weak.

KEY WORDS: MDR-TB, community base model, treatment outcomes.

This Article may be cited as: Khan MA, Basit A, Javaid A, Adnan MA, Ahmad F, Khan N, Khattak A, Sajjad H, Khattak MA. Outcome of community based therapy of multi drug resistant tuberculosis patients treated in a tertiary care hospital of khyber pakhtunkhwa. Pak J Chest Med 2014; 20(3): 81-85

INTRODUCTION

Despite the availability of effective chemotherapy for over 60 years, tuberculosis (TB) remains the leading killer of young adults throughout the world. The epidemiology of TB, with its persistence in poor countries and resurgence among the poor of many industrialized nations, is a cause of concern among the public health personnel. Two major factors responsible for this situation are; outbreak of HIV and emergence of Drug Resistance. Since 1997, when the first global surveillance of drug resistant tuberculosis (DR-TB) was reported, data on

the threat that drug-resistant TB poses to TB control internationally have been growing^{1,2,3}. Drug-resistant tuberculosis remains a growing threat to public health despite advances made in treatment and diagnosis over the past decade^{4,5,6,7}.

Treatment of MDR-TB remains challenging and complex, and treatment success is considerably lower than drug-susceptible TB⁸. Second line drugs (SLD's), used for treatment of MDR-TB are of very high cost and limited in number. In response to the high cost of these drugs and the lack of treatment options for MDR-TB patients, the World Health Organization

(WHO) along with other partners, launched the Green Light Committee (GLC) in 2000.⁹ The aim of launching of GLC was to facilitate the treatment of MDR-TB patients by extending existing directly observed treatment short-course (DOTS) programmes for TB treatment, termed DOTS - Plus. The threat of MDR and XDR tuberculosis could hardly have come at a worse time in the midst of the worst economic conditions in a century. In theory, the cost burden to developing countries for treatment of MDR and XDR cases may far exceed their total budgets for health care, and aid from the Global Fund to Fight AIDS, Tuberculosis, and Malaria or other sources will be essential for some time if we are to try to control this problem.

Detection and treatment of all forms of MDR-TB should be an integral part of NTP activities. Experience shows that developing capacity for MDR-TB management can strengthen the overall capacity of an NTP to implement TB control measures. The key actions for preventing and controlling drug-resistant TB include use of recommended treatment regimens, a reliable supply of quality assured first and second line anti TB drugs, and adherence to treatment by patients and close monitoring and supervision by health care providers. Pakistan ranks 4th among the MDR-TB high burden countries. The prevalence of MDR-TB was reported to be 1.8 % of all new smear positive TB cases in Pakistan¹⁰. The high rate of MDR and XDR-TB in Pakistan underscores the importance of effective treatment programs of drug-resistant TB. Expanding access to MDR- TB therapy is urgently needed, yet poor implementation of such therapy can worsen the problem of XDR-TB. Understanding risk factors for poor treatment outcomes among MDR-TB patients is necessary to improve treatment outcomes^{11,12}.

We therefore examined the MDR-TB patient registered in Lady Reading Hospital from 2008 – 2011 who received a second line therapy for MDR-TB to determine overall treatment outcomes.

MATERIAL AND METHODS

Location

The study was conducted in the Pulmonology department Lady Reading Hospital Peshawar. It is a cross sectional study involving review of all patients registered and treated for MDR-TB patients at DOTS Plus unit, Pulmonology Department, LRH, Pakistan from 1st October 2008 to 31st December 2011.)

Laboratory testing:

Sputum smear microscopy was done in microscopy laboratory in Chest ward and Cultures were processed at Agha Khan University Hospital, Karachi, using the direct proportion method with dilutions of culture inoculated onto Löwenstein-Jensen (LJ) media. DST against INH, RMP, PZA, EMB, ofloxacin (OFX), cycloserine (CS), ethionamide (ETH), and streptomycin (SM). DST against PZA was recognised to be unreliable. Careful attention was paid to the pH of LJ media for PZA testing (pH _ 5.5).

Chemotherapy Policy:

To be included in the study, patients required culture and drug susceptibility testing (DST). The initial diagnosis of TB was made by positive sputum smear and/or culture and sensitivity. Treatment was given as an outpatient and every patient was reviewed on monthly basis along with his treatment supporter. Standardized regimen was started initially while waiting for Culture and DST result. This regimen consisted of Aminoglycoside (Kanamycin), Fluroquinolones, Ethionamide and Cycloserine/PAS. Individually tailored regimens were selected for the patients on the basis of the results of in vitro susceptibility testing.

The drugs and the dosages used are listed in Table 1. We administered four drugs not given previously to which the tubercle bacilli were fully susceptible at the absolute concentration tested in vitro, including one parenteral agent (an aminoglycoside) and three oral agents that met these criteria.

Additional information in the computerized database included age, sex, weight, chest radiograph findings at initiation of treatment, sputum smear results, sputum cultures, all medications and their dosages, and outcome. While specific side effects were not recorded in the database, the need to interrupt or change medications due to side effects was recorded. Previous treatment was self-reported. Outcomes were cure, treatment completed, treatment failure, loss to follow-up and death. As cultures and DST availability were limited, treatment failure was determined by the treating physicians and was based on symptoms, sputum smears and chest radiograph response to treatment.

Support

This study was performed before the comprehensive PMDT was implemented which involves beside free drugs, free investigations, travel incentives, social support and involvement of district TB officers for supervision. Since our study was not supported by NTP we due to lack of resources only provided free drugs and no other support.

Definitions

Treatment outcomes were defined according to recommendations from the WHO MDR-TB working group¹⁸. Cure was defined as at least five negative sputum cultures in the last 12 months of treatment. A single positive culture was allowed if it was followed by a minimum of three negative cultures. Patients were classified as having completed treatment if there were insufficient bacteriological results to classify the patient as cured, but no evidence of treatment failure.

Treatment failure was defined as two or more positive cultures in the last 12 months of treatment, or if a medical decision was made to determine treatment due to poor response or adverse events.

Default was defined as an interruption of two or more consecutive months to treatment. Patients were recorded as dead if they died during treatment, regard-

less of the cause.

Statistical Analysis:

All data were analyzed using SPSS software (15.0 version).

RESULTS

Baseline Demographics and clinical characteristics

There were a total of 341 patients out of which 145 (42.8%) were males and 196 (57.2%) females (Table 2). The mean age was 29.15 (SD ± 13.211) years with age categorization was done as ≤ 30, 31 – 60 and 61 and above (Table 2). All the patients had their site of drug resistant tuberculosis in the lungs and all were HIV negative. The geographical spread of all the patients were from all over KPK but 141 (41.3%) patients

Table 1: Administered dosages of antituberculosis drugs in patients with MDR-TB

Drugs	Usual Dosage
Pyrazinamide	25-30 mg/kg daily by mouth
Ethionamide	15 mg/kg daily by mouth
Para-aminosalicylic acid	150 mg/kg daily by mouth
Cycloserine	15 mg/kg daily by mouth
Ofloxacin	15 mg/kg daily by mouth
Kanamycin	15 mg/kg by IM

Table 2: Characteristics of study samples

Variables		Frequency	Percent
Gender	Male	145	42.8
	Female	196	57.2
Age Group	≤ 30	221	64.8
	31 – 60	113	33.1
	61 Above	7	2.1
Treatment Outcomes	Cured	80	23.5
	Completed	134	39.3
	Default	50	14.7
	Failed	7	2.1
	Died	70	20.5
Previous Treatment	CAT I	92	27.0
	CAT II	239	70.1
	Repeat CAT II	10	2.9

were from inside Peshawar, the capital city and where this focal hospital is situated. The rest were scattered around various districts of KPK and FATA. A total of 223 (65.4%) patients were living in Rural Area whereas the remaining 118 (34.6%) patients were from urban areas. Most of the patients (70.1%) took category II treatment in their past whereas 27.0% took category I and 2.9% repeat category II treatment in the past.

High levels of first-line resistance were observed, with 288 (84.5%) out of 341 strains resistant to four first-line drugs tested. MDR (Resistance to RH) was found in 325 (95.3%), XDR was found in 2 (0.6%) strains, whereas 339 (99.4%) were resistant to Isoniazid, 326 (95.6%) were resistant to Rifampicin, 319 (93.5%) were resistant to pyrazinamide, 265 (77.8%) were resistant to ethambutol and 59 (17.3%) were resistant to streptomycin. Overall, 138 (40.5%) strains were resistant to at least one secondlineanti-TB drugs. The most common second-line resistance was to fluoroquinolones 127 (37.24%), followed by Ethionamide 13 (3.81%), amikacin 7 (2.05%), Kanamycin 6 (1.75%) and Capreomycin 6 (1.47%). Treatment outcome

134 (39.3%) patients had treatment completed, 80 (23.5%) were cured, 7 (2.1%) failed, 70 (20.5%) died during the treatment and 50 (14.7%) defaulted (Table 1). All the patients reported previous treatment of first line anti TB drugs out of which 28 (8.2%) treated with second line drugs.

DISCUSSION:

Community based management is an evolving mechanism for MDR-TB treatment supervision. This system is so far being used in some countries in the world and Pakistan is one of them. If we compare our treatment outcome results with a study conducted in Lima, Peru Mitnick C et al¹³ which was one of its first in respect to community based management of MDR-TB, the treatment success rate in our study was 62.8% whereas their treatment success was 83.0%. This was due to the fact that their treatment supervision were far better and surveillance for adverse events were managed by a team of specially trained community health workers, nurses and physicians.. In another study Kim HJ et al¹⁴ the treatment success rate was 48.5%, which is comparable to our study but their study was large with 1011 cases. Our results also suggest that around 80% of MDR-TB patients belong to the productive age group which can have serious socio-economic consequences. The overall success rate of 46% reports from other cohorts of MDR-TB is lower than our study^{15,16,17}, however, another meta analysis by Johnston et al, which include relatively higher burden countries including South Africa, found similar 62% success

rate¹⁸. By moving treatment into the community, it is possible, without compromising the quality of therapy, to lower costs and reduce the risk of nosocomial spread of multidrug-resistant tuberculosis. Treatment Failure among this cohort was 2.1% which is lower than 10% reported in the study of Farely J E et al¹⁹ Although the treatment success rate was comparable to some other studies published globally, however the death and default rate in this study was 20.5% and 14.7% respectively. These values which are on a high side need to be addressed and brought down through well integrated programme spearheaded by NTP.

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