Research Article

Treatment Outcome of Drug Resistant Tuberculosis Patients of Kashmir Valley by Molecular Assays: A prospective study

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Abstract

Objective/Background: Strains of drug-resistant tuberculosis are a major threat to global TB control disease centers. In the low and middle-income countries, it possesses great challenge due to underdeveloped health care system and resource constraints, which make it difficult to identify and monitor drug resistance cases using drug susceptibility testing and culture. Molecular assays such as CBNAAT, TRUENAT, GeneXpert and Line probe assays prove cost-effective solution to this problem in this setting. The objective of the study is to evaluate the use of molecular assays and Line probe assays in the diagnosis of pulmonary Tuberculosis and its drug resistance and treatment outcome in the patients of Kashmir valley. **Materials and Methods**: The present study was conducted in the Department of Chest Medicine, Chest Diseases Hospital (CDH), Govt. Medical College, Srinagar and Intermediate Reference Laboratory (IRL), State TB Training and Demonstration Centre (STDC), Chest Diseases Hospital, Srinagar and in association with State Tuberculosis office (STO) Kashmir. This is a three years prospective study involving patients who presented with clinically suspected TB or documented TB not improving on standard therapy and had samples sent on advanced testing, a total of 400 cases were taken for the study out of 195 reported drug resistance and sensitivity in the ethnic population. **Results**: In our study, 195 patients were treated for drug resistant tuberculosis between 2017 to 2021. Patients' age ranged from 25 to 80 years; 101 patients (51.8%) were male and 101 patients (51.8%) were living in rural areas. 135 patients were smokers, 13 patients had multidrug-resistant tuberculosis, 111 patients had rifampicin resistance and 42 patients had isoniazid resistance. Treatment outcomes of tuberculosis patients were as follows: 97 patients were cured (49.7%), 13 completed treatment (6.6%), 34 patients died before completing the treatment, 11 patients were lost to follow up (5.6%) and 1 patients had treatment failure. **Conclusion**: Treatment success outcomes occurred in more than half of the cases, which is lower than the World Health Organization target of at least a 75% success rate. A significant number of patients abandoned their treatment before its completion. These dropouts are a serious public health hazard that needs to be addressed urgently.

Keywords: Tuberculosis; RNTCP CBNAAT; LPA; Resistance; Kashmir

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Introduction

Drug resistance tuberculosis (TB) is a major threat to TB control programme of the worldwide. It is a global health challenge putting an extra burden on the health care system and economies of countries, especially in low and middle income countries where there is no advanced and systematic health care system and different cultural ethos are prevalent. [1,2] TB is a ranked among the ten causes of death worldwide and as a one of the leading causes of death from infectious disease. India accounts for 1/4th of the global tuberculosis burden and it is reported that around 4.8 lakh people died due to TB of estimated 28 lakh infected cases in 2015. [2,6] Tuberculosis (TB) is caused by infection with Mycobacterium tuberculosis, which is transmitted through inhalation of aerosolized droplets. It mainly attacks the lungs, but can also affect other parts of the body like brain, kidney, and spine. [7] TB is highly contagious during the active phase of the disease and can infect an individual through inhalation of as little as ten Mycobacterium tuberculosis (MTB) bacteria. [7] After inhalation, these bacteria are mainly apprehended by the alveolar macrophages, but they can dodge the host immune system and remain in the dormant phase for a long period of time, at which point they can reactivate to a virulent form under immune-compromised situations of the host. The bacterium can persist in slow growing as well as in fast growing stages which makes treatment challenging. Almost all of the antibiotics that can be used to treat TB work when the bacteria are actively dividing. In the intensive phase of TB treatment, the antibiotics mainly kill rapidly growing bacteria, which causes rapid sputum conversion, and the eradication of clinical symptoms. However, in order to kill the persistent or slow growing strains of MTB, the continuation phase of the treatment is essential. TB can be treated effectively by using first line drugs: isoniazid, rifampin, pyrazinamide, ethambutol and streptomycin. However, this first line therapy often fails to cure TB for several reasons. [8] Relapse and the spread of the disease contribute to the emergence of drug resistant bacteria. [9] The emergence of multidrug resistant TB (MDR-TB), i.e. which is resistant to at least isoniazid and rifampicin , is of great concern, because it requires the use of second-line drugs that are difficult to procure and are much more toxic and expensive than First line defense drugs. [9] Therefore, the detection and treatment of drug susceptible or single drug resistant TB is an important strategy for preventing the emergence of MDR-TB. [10] M. tuberculosis strains with extensively drug resistant-TB (XDR-TB), that is resistant to isoniazid or rifampicin (like MDR tuberculosis), any fluoroquinolone, and at least one of three second-line anti-tuberculosis injectable drugs i.e., capreomycin, kanamycin, and amikacin have also been reported. [6] The tuberculosis disease is treatable and curable except for those people who don't get proper treatment on time will have cent percent mortality chances. Its mortality rate is associated with the treatment. [11] Also, sometimes some strains show resistance to drugs available in the treatment line, which means that the drug is not enough capable to kill the mycobacterium tuberculosis. Drug resistance is caused by a mycobacterium which is resistant to at least one first-line anti-TB drug. [2] Multi-drug resistant tuberculosis (MDR-TB) is defined as resistance to isoniazid and rifampicin, the most potent anti-TB drugs, while extensively drug-resistant tuberculosis (XDR-TB) is defined as MDR-TB with additional resistance to any second-line drugs. Rifampicin resistance (RR) is used as a proxy for MDR-TB and rapid detection of RR strains is recommended. [10,11] The possible cause of the sudden emergence of drug resistance in Mycobacterium tuberculosis has been associated with different factors like management issues and patient care in the TB control programmes. The (i) poor holding cases, (ii), sub-standard drugs, inadequate or irregular drug supply and lack of supervision; (iii) ignorance of health care workers in epidemiology, treatment and, control; (iv) improper prescription of regimens; (v) non-adherence of patients to the prescribed drug therapy; (vii) availability of anti-TB drugs across the counter, without prescription; (vi) massive bacillary load; (vii) illiteracy and low socio-economic status of the patients; (viii) laboratory delays in identification and susceptibility testing of Mycobacterium tuberculosis isolates; (ix) use of non-standardized laboratory techniques (12). Drug resistance in Mycobacterium tuberculosis occurs by random or by spontaneous mutation at a low frequency, in large bacterial populations. [12] It has been reported that probability of incidence of drug-resistant mutants is 10-8 for rifampicin, while for isoniazid and other commonly used drugs is 10-6. Therefore, the probability for resistance to both isoniazid and rifampicin to develop is [10-14], which is much larger than the number of organisms present in a medium-sized cavity in a patient with open pulmonary TB. [12] Advanced CBNAAT and TRUENAT nucleic acid amplification technology aids in the detection of drug resistance of mycobacterium in tuberculosis patients. Molecular assays such as CBNAAT, TRUENAT, and LPA are changing the landscape of the diagnosis and management of drug-resistant TB and may prove to be a cost-effective solution to this problem in a variety of settings. CBNAAT/TRUENAT (GeneXpert) molecular testing uses real-time polymerase chain reaction to detect the specific sequence for Mycobacterium tuberculosis as well as that for rifampicin resistance and can supplement standard diagnostic tools (such as the acid-fast stain in the Kashmir population). Line probe assays are drug susceptibility tests that use PCR and reverse hybridization methods for the rapid detection of mutations associated with drug resistance. Line probe assays are designed to identify Mycobacterium tuberculosis complex and simultaneously detect mutations associated with drug resistance. Since the endorsement of molecular assays by WHO in 2010, over 110 low- and middle-income countries have purchased GeneXpert, many of which have incorporated it into their diagnostic algorithms for TB. [12] Preliminary findings have been promising, showing that more cases of TB are being identified (including MDR-TB), there is a shorter time-to-treatment initiation, and TB diagnosis is becoming decentralized. Hence, the objective is to evaluate the drug

resistance and treatment outcome pattern in pulmonary tuberculosis patients of Kashmir valley.

Methodology

Study Setting: This hospital-based study was conducted in the Department of Chest Medicine, Chest Diseases Hospital (CDH) Govt. Medical College, Srinagar and Intermediate Reference Laboratory (IRL), State TB Training and Demonstration Centre (STDC), Chest Diseases Hospital, Srinagar.

Study Design: Observational prospective study.

Ethical clearance: After acquiring the formal ethical clearance from the institutional ethical Committee of Government Medical College Srinagar under Ref No: 138/ETH/GMC/ICMR, a study was conducted on the ethnic population of Kashmir from March 2019 to March 2021.

Age group: Patients older than 25 years were taken for the study after getting due consent. The sample size was estimated based on World Health Organization's (WHO) guidelines.

Sample size: A total of 400 patients were selected for the study with sex and age-matched. A prospective analysis was performed regarding the treatment outcome of 400 cases of pulmonary tuberculosis registered under RNTCP (Revised National Tuberculosis Programme) from March 2019 to March 2021. Data was collected from patients enrolled for directly observed treatment short-course (DOTS) at the hospital. All registered MDR/ XDR TB cases were treated with the appropriate dosage of drugs per the sensitivity panel and followed up regularly. The diagnosis was based on clinical features, chest radiography, sputum microscopy, and other supportive laboratory parameters. Among 400 cases, 195(48.7%) were sputum smear-positive. Cases were put on the recommended anti-TB treatment regimen.

Inclusion Criteria: Patients from Kashmiri Origin, Pulmonary Tuberculosis Patients with Drug resistance.

Exclusion Criteria: Patients having any underlying disease like diabetes, cancer etc., Non-Kashmiri origin, HIV.

Diagnosis and Drug Resistant TB Treatment: The survey tool consists of patient's socio-demographic details and laboratory examinations. The participants having symptoms like cough>2 weeks, chest pain, fever more than two weeks, diabetes, and age>65 years were taken for sputum examination and were asked to provide two sputum samples as per WHO criteria. X-ray examinations were done at the nearest facility and the suspicious X-ray reports were tested using Acid-fast bacillus (AFB) staining and were further confirmed by advanced technologies of diagnostics i.e. Cartridge Based Nucleic acid Amplification Test (CBNAAT) / True Nat and LPA. Patients who were found positive were given treatment at the nearest hospitals using Directly Observed Treatment Short-course (DOTS).

All patients diagnosed with resistant TB during the study were included. The diagnosis was done by GeneXpert / CBNAAT/True Nat/LPA and drug susceptibility testing (DST) for first-line anti-TB drugs (rifampicin, isoniazid, streptomycin, pyrazinamide and ethambutol) and second-line anti-TB drugs (ofloxacin, kanamycin and capreomycin). All DR-TB patients were tested for HIV at baseline. DR-TB regimen consisted of an intensive phase lasting a minimum of 6 months and consisting of an injectable agent (kanamycin or capreomycin), in addition to levofloxacin, ethionamide, pyrazinamide, ethambutol and vitamin B_6. It was then followed by the continuation phase during 18 months and consisting of the regimen prescribed for the intensive phase without the injectable agents. The duration of DR-TB treatment was 24 months. All drugs were administrated under directly observed therapy (DOT). Sputum smears and molecular assays were obtained monthly during the intensive phase of DR-TB treatment. Drug sensitivity testing (DST) was done for First line Anti-tuberculosis therapy regimen mainly Rifampicin (RIF) and Isoniazid (INH) resistance by using Line probe assay (LPA) and second line ATT by Cartridge based nucleic acid amplification test (CBNAAT) and TrueNat. These molecular tests identify Mycobacterium tuberculosis (MTB) and simultaneously detect mutations associated with drug resistance. The aim of the study was to detect the drug resistance and sensitivity profiling in pulmonary tuberculosis patients of Kashmir valley by molecular assays.

Treatment outcomes: Treatment outcomes were defined and classified according to the WHO guidelines. [13] Cured from DR-TB was defined as those who completed treatment within 18 months to over 2 years, followed by at least two negative sputum cultures. Completed treatment was defined as patients who completed the anti TB regimen for at least 18 months. Death was defined as patients who died during treatment whatever the cause.

a. Failed treatment was defined as smear positive patients who remained positive at the fifth month of treatment or smear negative turning positive.

b. Lost to follow-up was defined as treated patients who did not come back to complete chemotherapy and there was no evidence of cure through the sputum result during the fifth month of therapy. Treatment interruption was defined as patients who did not collect medications for 2 months or more at a particular time or only intermittently, but still came back for treatment and in the 8th month of treatment their sputum result was positive.

c. TB relapse refers to patients who had previous TB treatment and were cured but were diagnosed again with a new TB infection.

d. Successful treatment outcomes include cured patients and those who completed treatment. Poor treatment outcomes include death, TB relapse, loss to follow-up and failure to complete treatment regimen. [8]

Data collection: A data collection in terms of questionnaire was designed using the medical history of all the patients diagnosed with resistant TB during the study period. DR-TB

was confirmed by drug susceptibility testing (DST) for first-line anti-TB medicines and for second-line medicines. Patients included received second-line anti-TB medicines including ethionamide, kanamycin or capreomycin, and ofloxacin. The duration of treatment was 24 months. All socio-demographic and clinical data were prospectively collected: age, gender, residence, marital status, employment, comorbidity, TB drug resistance types, smoking habits, culture positivity, smear positive pulmonary tuberculosis (PTB+) at baseline, and treatment outcomes.

Data Analysis

The data was entered in the MS Excel work spread sheet 2011. The SPSS 2016 (Chicago, IL) programme was used for stastical analysis. The clinical information and laboratory data were expressed and analyzed on per patient basis. For comparisons between groups, paired and unpaired students to test were applied using a significance level of $p=0.05$, $p<0.05$ was taken stastically significant.

Results

A total of 400 participants were enrolled in this study (Table 1). The mean ± standard deviation (SD) age of participants was 47.5 ± 15.45 years. Out of enrolled 400 cases, 205 (51.25%) cases were TB negative by Acid Fast Bacillus staining method and 195(48.7%) cases were smear TB positive by Acid Fast Bacillus. Further, 195 cases were selected as per WHO criteria for drug resistance/sensitivity profiling, among which, 94 were women (48.2%) and 101 were men (51.8%) in the study, also they met inclusion criteria. There were 120(61.5%) drug resistant patients who had a positive history of household TB contact. The socio-demographic and clinical characteristics are elaborated in the (Table 1).

Table 1: Socio-Demographic characteristics of drug resistance tuberculosis patients.

Characteristics	N (%)
Total Number of Subjects	400 (100)
Patients with Smear Positive and confirmed DR	195 (48.7)
Patients With Smear Negative	205 (51.25)
Age (mean ± SD)	47.5 ± 15.4
Age Group (Years)	90 (46.1)
< 40	105 (53.8)
>40	
Gender	101 (51.8)
Male	94 (48.2)
Female	
Residence	94 (48.2)
Urban	101 (51.8)
Rural	
Occupational status	20 (10.2)
Salaried Class	45 (23.0)
Business Class	100 (51.2)
Labour Class	30 (15.3)
Un-employed	
Educational status	55 (28.2)
Educated	145 (74.3)
Illiterate	
Economic status	95 (48.7)
Above Poverty Line (APL)	100 (51.2)
Below Poverty Line (BPL)	
Marital Status	155 (79.4)
Married	35 (17.9)
Un-Married	05 (2.5)
Divorced/separated	
Smoking Habits	135 (69.2)
Smokers	60 (30.7)

Non-smokers	
Smear TB Positive	184 (94.3)
Pulmonary	11 (5.6)
Extra-Pulmonary	
TB contact	120 (61.5)
Household	75 (38.5)
Another	
Duration of TB Disease	101 (51.7)
<5 years	94 (48.2)
>5 years	
Patients on DOTS	125 (64.1)
<2 years	70 (35.8)
>2 years	
Type of Base line Drug resistance	175 (89.7)
First Line ATT	20 (10.2)
Second Line ATT	

Majority of patients were>40 in age (n=105, 53.8%) having rural dwelling (n=101, 51.8%), most of the patients were belongs to Labour class (n=100, 51.2%) and economically were settled in below poverty line (n=100, 51.2%). As per educational status and smoking, 145(74.3%) were illiterates and 135 (69.2%) were smokers. The patients on first line ATT therapy were 175 (89.7%), also 125 (64.1%) were relying on ATT treatment below<2 years duration. Sensitivity and resistance to first-line Anti tuberculosis treatment (ATT) drugs were analyzed in (Table 2).

Table 2: Drug resistance and sensitivity profiling to first line anti-tuberculosis therapy (N=195).

Drug	Resistance (n%)	Sensitivity (n%)
Isoniazid+Rifampicin (MDR*)	13(6.6)	15(7.6)
Rifampicin	111(56.9)	5(2.5)
Isoniazid	42(21.5)	8 (4.1)
Streptomycin	7(3.5)	40(20.5)
Ethambutol	2(1.0)	75(38.4)
Pyrazinamide	1(0.5)	45(23.0)
Streptomycin+Isoniazid+Rifampicin+ethambutol (SHRE)	11(5.6)	5(2.5)
XDR*	8(4.1)	2(1.0)

*MDR= Multi-Drug resistance, XDR= Extensively Drug Resistant.

Most of the TB cases (n=111; 56.9%) were resistant to Rifampicin but were sensitive to ethambutol (n=75; 38.4%). There were 6.6% (n=13) cases of MDR-TB. All these patients were being treated with first-line ATT. Among the cases of MDR-TB, there were 7 (53.8%) men and 5 (38.4%) women. The patients resistant to Isoniazid drug in our study is 42 (21.5%) and 45 (23.0%) reported sensitivity to Pyrazinamide. Besides this, patients under the SHRE reported 5.6% (n=11) drug resistance and 2.5% (n=5) are sensitive to SHRE. In the XDR category, 4.1% (n=8) are resistant and 1% (n=2) are reported to be drug sensitivity in first line ATT (Figure 1(A), Figure 1(B), Figure 1(C)).

Table 3: Drug Resistance and Sensitivity profiling to Second line Anti-tuberculosis therapy (N=33).

Drug	Resistance (n%)	Sensitivity (n%)
Fluroquinone	8(24.2)	4(12.1)
Oflaxcin	18(54.5)	4(12.1)

Ethionamide	3(9.0)	15(45.4)
Capreomycin	4(12.1)	12(36.3)

The Thirty Three (n=33) number of patients reported drug resistance to MDR; SHRE and XDR drugs of ATT were further treated with second line. Regarding the second-line therapies, many TB cases (n=18; 54.5%) were resistant to ofloxacin while most were sensitive to Ethionamide (n=15; 45.4%), Capreomycin (n=12; 36.3%). The sensitivity and resistance patterns for second-line ATT are shown in (Table 3).

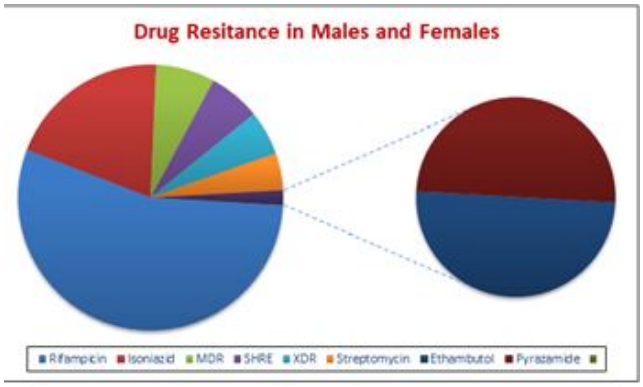

Figure 1(A): Pie-chart representing drug resistance pattern among males and females.

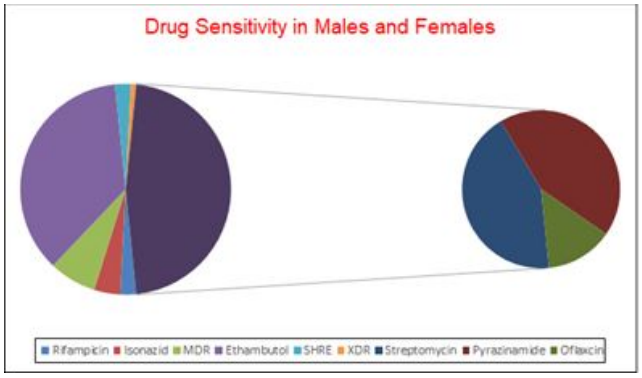

Figure 1(B): Pie-Chart representing Drug Sensitivity pattern among males and females.

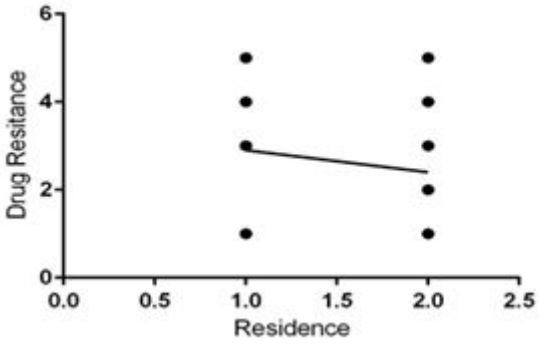

Figure 1(C): The linear regression analysis of drug resistance pattern among urban-rural population of Kashmir, reported non-significant association ($p<0.05$). The pattern analysis of drugs was analyzed on the basis of data in (Table 2) and (Table 3).

*(R-square= 0.0308, 95% CI= -1.063-0.06282, P=0.0806)

Table 4: Tuberculosis treatment outcomes according to baseline drug resistance patterns.

Outcomes	Drug resistance to isoniazid	Drug resistance to Rifampicin	Drug resistance to E +P+S*	SHRE*	MDR*	XDR*	Total
Number of Cases	n=42	n=111	n=10	n=11	n=13	n=8	N=195
Positive outcomes							
Cured	25 (59.5)	55 (49.5)	2 (20)	8 (72.7)	6 (46.1)	1 (12.5)	97 (49.7)
Treatment Completed	1 (2.3)	10 (9.0)	0 (0)	0 (0)	2 (15.3)	0 (0)	13 (6.6)
Successful treatment (Cured +Completed)	26 (61.9)	65 (58.5)	2 (20)	8 (72.7)	8 (61.5)	1 (12.5)	110 (56.4)

Negative outcomes							
Failure	0 (0)	1 (0.9)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.5)
Died	1 (2.3)	22 (19.8)	0 (0)	3 (27.2)	2 (15.3)	6 (75)	34 (17.4)
Lost to follow up	0 (0)	11 (9.9)	0 (0)	0 (0)	0 (0)	0 (0)	11 (5.6)
Transfer out	0 (0)	14 (12.6)	0 (0)	0 (0)	2 (15.3)	0 (0)	16 (8.2)
Poor Treatment (Failure+Death+ Lost to Follow-up+ Transfer out)	1 (2.3)	48 (43.2)	0 (0)	3 (27.2)	4 (30.7)	6 (75)	62 (31.8)

*E= Ethionamide, P=Pyrazinamide, S= Streptomycin.

It is summarized here that the Treatment outcomes of our 195 drug resistant TB patients were as follows: 110 had successful treatment (56.4%), 97 were cured (49.7 %) and 13 completed treatment (6.6%). Poor treatment outcome was seen in 62 patients (31.8%), 34 patients (17.4) died before completing treatment, 1 patients had treatment failure (0.5%) and 11 patients were lost to follow-up (5.6%) (Table 4).

Discussion

The emergence of drug resistance is a worrisome problem which poses a formidable challenge to physicians across the world and hinders effective TB control. Treatment of MDRTB is complex due to the prolonged regimens, expensive drugs, and high incidence of drug toxicities. This is, in turn, contributes to poor treatment adherence and further exponential magnification of drug resistance which can have devastating consequences. In India, MDRTB has been persistently identified despite the successful implementation of RNTCP. As per recently published reports from India, MDRTB has been found in 3% of new cases and 12% of treated patients. [14] Formulation and implementation of PMDT guidelines are milestone achievement to combat this challenging problem. This is the first study in the Kashmir valley that evaluates treatment outcomes of DR-TB and drug resistance and sensitivity in the line of ATT therapy in ethnic population. Of the 195 DR-TB patients in this study only 110 (56.4%) were successfully treated; these outcomes were lower than the 2019 WHO target for MDR TB of at least 75% treatment success. [15] In our study, the majority of patients were males (54.8%) which are in accordance with other studies that found that DR-TB is more common in males. [16-19] Most of our patients are young, with a mean age of 47.5 years, in agreement with the study of who found a mean age of 39.35 years. [20] Labor class and un-employed was noted in 51.2% and 15.3% of the patients, which is in line with the study of Marta Gomes et al who found 51.8% were unemployed patients. [20] DR-TB is frequently seen in patients who have low socioeconomic status and who are illiterate and unaware of the risks to others as well as to themselves. According to TB drug resistance types, the majority of patients were rifampicin resistant, Isoniazid resistant and MDR Resistant. This is in agreement with who found 76.1% of patients with DR-TB were MDR-TB. [21] Successful treatment outcomes in our study were slightly lower than those found in studies done in Shanghai, New York and Hamburg, (54.9, 64% and 80% respectively). [22-25] But, they were higher than those found in studies done in Ukraine, South Korea and South Africa (18%, 48.2% and 49% respectively). [26-28] The success rate in our study was higher than the one found [29,30] who found a success rate of 17.1% and 39% respectively. One of the most serious obstacles for TB control efforts is the low rate of treatment success among DR-TB patients as this might lead to the development of more resistance and the transmission of these more resistant strains to other persons. The major factor hindering treatment success is the high number of patients who are lost to follow-up. [31] In our study, we found 5.6%, which was a low loss to follow-up rate. This rate was lower than in studies done in Pakistan, Spain, South Africa and South Korea which found a loss to follow- up rate of 1.1%, 16%, 29% and 32% respectively. [32–34] Among possible reasons for loss to follow-up or discontinuation of therapy in our study were the adverse drug reactions, the long duration of treatment and an improvement in symptoms. The study of [37] highlighted lack of patient-provider interaction, drug use, and socioeconomic characteristics as the most significant factors associated with loss to follow-up. In our study, the failure rate of 0.5% was lower than the 8% and 8.7% failure rates found in 2 other studies of DR-TB patients. [38,39] The mortality rate was higher 15.3% and the findings. Who found 5% of death among MDR-TB patients? [40] In our study, smoking habits were associated with poor treatment outcomes, these results are in accordance with the results of the study of [41] and a study conducted by [42], and they evaluated the association of smoking and unsuccessful treatment outcomes among TB patients.

Conclusions

In conclusion, in Kashmir valley, the treatment strategy was effective for susceptible TB and for mono- and poly-drug resistant TB but not for MDR-TB. Ensuring adherence to long and poorly effective treatment regimens, especially for patients living in difficult socio-economic conditions, is a real challenge in Kashmir. Large metacentric cohort analyses are required to further investigate optimal treatment regimens

for MDR-TB with existing drugs. The evidence of MDR-TB nosocomial transmission emphasizes the paramount importance of infection control in hospitals and of more decentralized and outpatients approaches for treating drug resistant TB. In high MDR burden and limited resource countries, the programmatic impact of using the new molecular methods (eg. GeneXpertMTB/CBNAAT/TRUENAT/LPA), which does not require heavy laboratory infrastructure, should be assessed. Indeed, these methods would allow faster identification of rifampicin resistance in both smear-positive and smear-negative patients, and a more rapid initiation of empirical MDR regimen, while waiting for full DST results. It is likely that earlier Rifampicin/MDR treatment would reduce the fatality rate. GeneXpertMTB/LPA was recently introduced in the Kashmir valley. The incidence of MDR-TB is alarmingly high. The amplification of TB awareness and management programs, along with rigorous infection control measures, are crucial for putting an end to this emerging health concern. MDR-TB detection and awareness programs must be of high quality, and treatments should be based on globally recommended regimens such as WHO guidelines.

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