Scholars Journal of Applied Medical Sciences (SJAMS) **ISSN 2320-6691 (Online)**
Sch. J. App. Med. Sci., 2016; 4(3C):820-827 **ISSN 2347-954X (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublishers.com DOI: 10.36347/sjams.2016.v04i03.041

Original Research Article

A Study to assess the profile of multidrug-resistant tuberculosis (MDR-TB) in tertiary care hospital setting

Dr. Vikas Kumar Mishra[1], Dr. Prerna Gupt[2], Dr. Pradeep Pachar[3], Dr. Suresh Kumar Jangir[4], Dr. Rakesh C. Gupta[5], Dr. Neeraj Gour[6]

[1]Senior Resident, LN Medical College, Bhopal, Madhya Pradesh, India
[2]Medical Officer, Govt CHC, Chomu, Rajasthan, India
[3]Medical Officer, Divisional Railway Hospital, Ajmer, Rajasthan, India
[4]Medical Officer, TB-Sub Clinic, Govt District Hospital, Churu, Rajasthan, India
[5]Ex Prof & Head, Dept of Respiratory Medicine, J.L.N. Medical College & Associated Group of Hospitals, Ajmer, Rajasthan, India
[6]Associate Professor, Dept. of Community Medicine, SHKM Govt. Medical College, Mewat, Haryana, India

***Corresponding author**
Dr. Neeraj Gour
Email: drneeraj_g04@yahoo.com

Abstract: Drug resistance is a threat to TB control programs worldwide. Patients infected with multiple-drug resistant strains are less likely to become cured. This study was conducted to assess the profile of multidrug-resistant tuberculosis (MDR-TB) in tertiary care hospital setting, Ajmer, Rajasthan India. In methodology A total of 244 cases of Multidrug Resistant Pulmonary Tuberculosis registered under RNTCP (Revised National Tuberculosis Programme) for Cat IV regimen from 1st January 2012 to 30th September 2012 at PMDT site at Department of Respiratory Medicine, JLN Medical College and Associated Group of Hospitals, Ajmer, Rajasthan were included results Out of 244 patients, 62 (25.4%) patients belong to MDR Suspect Criteria A, 176 (72.1%) patients belong to MDR Suspect Criteria B, and 6 (2.5%) patients belong to MDR Suspect Criteria C. Out of 244 patients, 60 (24.6%) patients had documented h/o contact with TB patients, of which 53 (88.3%) patients had h/o contact with PTB patients, whereas 7 (11.7%) patients had h/o contact with MDR TB patients. According to radiological finding, 224 (91.8%) patients had bilateral lung disease, while 20 (8.2%) patients had unilateral lung disease. In conclusion the Health education regarding spread of disease, early detection of MDR-TB by strengthened laboratory support, effective therapy, implicating innovative control measures, and applying them specially among immigrants, would interrupt the ongoing transmission and control this emerging epidemic.
Keywords: tuberculosis, multidrug-resistant tuberculosis.

INTRODUCTION

Drug resistance is a threat to TB control programs worldwide. Patients infected with multiple-drug resistant strains are less likely to become cured [1] , The treatment is much more toxic and much more expensive than the one of patients with sensitive organisms [2] Presently, drug resistant mycobacterium tuberculosis is an important global threat, with a median of 9.9% of M. tuberculosis strains now resistant to at least one drug in 35 countries or regions [3]. A case of MDR-TB is about 20-40 times more expensive to manage than a case of drug-sensitive tuberculosis and patient suffering is also magnified [4].The prevalence of MDR-TB mirrors the functional state and efficacy of tuberculosis control programmes and realistic attitude of the community towards implementation of such programmes in the country [1].

Multidrug Resistant Tuberculosis (MDR-TB) has emerged as a significant global health concern. Globally, 3.7% (2.1-5.2) of new cases and 20% (13-26%) of previously treated cases are estimated to have MDR-TB. By the end of 2011, India and the Russian Federation, which combined with China, contribute to almost 60% of the estimated global burden of MDR-TB [5]. Extensively drug-resistant TB, or XDR-TB, has been identified in 84 countries; combining their data, the average proportion of MDR-TB cases with XDR-TB is 9% (6.7-11.2%) [5].

India has one-fifth of the world's Multidrug resistant TB burden – the largest number for any country globally after china [6]. Based on the results of Gujarat, Maharashtra and Andhra Pradesh DRS Survey, Estimated proportion of MDR-TB is 2.1% (1.5%-2.7%)

in New TB cases and 15% (13%-17%) in previously treated cases. As compared to global rates, the proportion of MDR-TB is lesser in India [7]. The emergence of MDR TB is a global problem, which is threatening to destabilize the best efforts of TB control [8, 9]. MDR-TB is a great challenge to clinicians for both diagnosis and Management. It is among the most worrisome element of the Pandemics of antibiotic resistance because MDR-TB patients that fail treatment have a deadly outcome [10, 11]. Currently only a little numbers of the existing MDR-TB patients are being diagnosed due to severe laboratory constraints all over the world, especially in low income countries.

We have planned to conduct this study, as limited data is present on category IV regimen in MDR TB patient, in the department of Respiratory Medicine, Jawaharlal Nehru Medical College Ajmer to study the profile of Multi Drug Resistant Tuberculosis (MDR TB) patients on Cat IV regimen under Revised National Tuberculosis Control Program (RNTCP) at treatment completion.

MATERIAL AND METHOD

It was a hospital based descriptive observational study 244 cases of pulmonary tuberculosis of Multidrug Resistant Pulmonary Tuberculosis registered under RNTCP (Revised National Tuberculosis Programme) for Cat IV regimen from 1st January 2012 to 30th September 2012 at PMDT site at Department of Respiratory Medicine, JLN Medical College and Associated Group of Hospitals, Ajmer, and Rajasthan. Informed consent of the patient was taken for the study. Approval from institutional ethical committee was obtained.

Inclusion criteria:

The patients with documented evidence of drug resistance to Rifampicin alone or along with Isoniazid from an Intermediate Reference Laboratory were included in the study. Following methods were used for Mycobacterial Culture & Sensitivity-

1. Conventional solid egg-based Lowenstein-Jensen (LJ) media
2. Molecular Line Probe Assay

In Ajmer, at State Tuberculosis Training and Demonstration Centre, Mycobacterial Culture and Drug sensitivity is done using Molecular Line Probe Assay. The negative samples from MDR suspect patients on LPA were subjected to culture on conventional solid egg-based Lowenstein-Jensen (LJ) media and DST was performed for Streptomycin (S), Isoniazid (H), Rifampicin (R), Ethambutol (E) and Pyrazinamide (Z).

Exclusion criteria:

All patients included and admitted for DOTS PLUS treatment were included for study. All patients who were found to have MDR TB were hospitalized at PMDT site, department of respiratory medicine, J.L.N medical college Ajmer for pre treatment evaluation and initiation of category IV regimen, for a minimum duration of seven days. The protocol was clearly explained to patient/care provider before enrolment and informed consent was taken from each patient.

Demographic characteristics, socioeconomic status, complete detailed clinical history regarding total duration of illness, smoking history, drug/alcohol abuse, mental illness, diabetic history, previous anti tuberculosis therapy, family history of anti tuberculosis therapy and any contact with tuberculosis patients were taken from the patients.

Health education and counseling was given to all patients including family members about the disease, about the necessity of taking regular and adequate treatment at different levels including at our centre, at district tuberculosis centers and also at their home by DOT providers.

After six months of intensive phase, patients were switched to continuation phase if 4th or 5th month culture report was negative. Intensive phase was extended for one month in one time for a maximum of three months until the negative culture report. Those patients who have taken nine months of intensive phase treatment were switched to continuation phase regardless of culture report.

Baseline datas with specific reference to previous history of ATT, pattern of drug resistance, extent of disease clinical as well as radiological, associated co-morbid conditions, socio economic status, addiction habits, body mass index (BMI) and baseline haematological investigations as per RNTCP guidelines were collected from records available at PMDT site.

All information to accomplish objective was collected by personal interview of study subjects at PMDT site using pre-designed proforma. Subjective perception of improvement and no improvement was criteria for clinical outcome in the form of improvement and no improvement (deterioration). In skiagram chest interpretation and analysis, opinion from consultant of our department was taken.

Statistical Analysis:

Data thus collected was entered into Microsoft excel worksheet in the form of master chart. Microsoft word and Excel have been used to generate graphs, tables etc**.**To find out significance of difference in proportions in various groups Chi square test was applied and for the significance cut off of P value <0.05 S was accepted as follows:

RESULT

Out of 244 patients who were included in the study population (74.6%) patients were in the age group of 16 - 45 years. Majority of cases were males (79.92%), with male: female sex ratio of 4:1. Most of the patients (92.2%) were married; only (7.8%) were unmarried. Most of the patients (94.7%) belong to three districts namely Ajmer, Nagour, Bhilwara included in the Ajmer zone. The Ajmer district comprises highest number of patients (42.2%). These districts are now shifted under PMDT Site started in Jodhpur and thereafter MDR TB patients from these districts were admitted at PMDT Site Jodhpur. However patients from these districts admitted at PMDT Site Ajmer are still included in Outcome Analysis. In our study (76.2%) patients belong to upper lower class, 26 (10.7%) patients belong to lower class, while patients belonging to Lower middle and upper middle socio economic classes were 25 (10.2%) and 7 (2.9%) respectively. Out of 244 patients, (29.9%) patients were educated only up to primary school,(6.1%) patients had completed Middle school,(2.9%) patients had high school certificate, 7 (2.9%) patients were graduates, while only (1.6%) patients had post graduate degree, (56.5%) patients were illiterate. Thus about half of the males and more than 80.0% of the females were illiterate in the study group.

Table 1: Socio-demographic profile of the study population

Demographic Variable	Total No Of cases (N=244)	Percentage
Age Group		
<15	3	1.23
16-25	49	20.08
26 -35	71	29.10
36 -45	62	25.41
46-55	36	14.75
56-65	20	8.20
66-75	3	1.23
Sex		
Male	195	79.92
Female	49	20.08
Marital status		
Unmarried	19	7.79
Married	225	92.21
Area		
Rural	192	78.69
Urban	52	21.31
	244	100.00
Socio economic status		
Lower	26	10.66
Upper lower	186	76.23
Lower Middle	25	10.25
Upper Middle	7	2.87
Education		0.00
Illiterate	138	56.56
Primary	73	29.92
Middle	15	6.15
High	7	2.87
Graduate	7	2.87
Post Graduate	4	1.64

Out of 244 patients, 192 (78.7%) patients were from rural population and 52 (21.3%) patients belong to urban areas. Most of the patients were Farmers (n=60, 24.6%), followed by manual laborers (n=42, 17.2%). Sixteen patients (6.6%) were drivers; seven patients (2.9%) were professional. Thirty eight patients (15.6%) were house wives, and 14 patients (5.7%) were student in this study. Out of 244 patients, 145 (59.43%) patients had history of addiction to smoking, alcohol and others, whereas 99 (40.6%) patients had no history of addiction. Out of 244 patients, 110 (45.08%) patients were smokers, 61 (25.0%) patients were alcoholic, 31 (12.7%) patients were tobacco chewer, 4 (1.64%) patients were opium abusers.

Table 2: Personal History (type of addiction and BMI) of the cases

Type Of addiction	**(N=244)**	%
No history of addiction	99	40.57
Smoker alone	57	23.36
Alcohol & smoker	38	15.57
Tobacco chewer alone	16	6.56
Alcohol alone	15	6.15
Smoking & Tobacco chewer	8	3.28
Alcohol ,Smoking & Tobacco chewer	4	1.64
Alcohol & Tobacco chewer	3	1.23
Smoking & Opium	3	1.23
Alcohol & Opium	1	0.41
Body mass index		
Normal	26	10.66
Underweight	218	89.34

It was found that majority of the patients, 218 (89.3%) were underweight, while 26 (10.7%) patients had normal BMI. None of patient was overweight. The distribution was almost equal among male and female patients. Out of 244 patients, 62 (25.4%) patients belong to MDR Suspect Criteria A, 176 (72.1%) patients belong to MDR Suspect Criteria B, and 6 (2.5%) patients belong to MDR Suspect Criteria C.

DST results on Molecular LPA were available for 241 patients. Out of 241, 160 (65.6%) patients were HR resistant and 81 (33.2%) were Rifampicin mono resistant. DST results on Conventional LJ media were available only for 3 patients and showed HRE resistance in 1 patient and SHR resistance in 2 patients.

Table 3: Diseases status of the cases

Suspect Criteria	**(N=244)**	%
A	62	25.41
B	176	72.13
C	6	2.46
Drug		
HR	160	65.57
R	81	33.20
HRS	2	0.82
HRE	1	0.41
No H/O Contact	184	75.41
H/O Contact with PTB	53	21.72
H/O Contact with MDR TB	7	2.87
Co- Morbidities Status		
Present	148	60.66
Absent	96	39.34
Radiological Findings		
Cavitatory Disease	209	85.66
Non Cavitatory	35	14.34
lesions		
MINIMAL	15	6.15
Moderately Advanced	95	38.93
Far Advanced	134	54.92

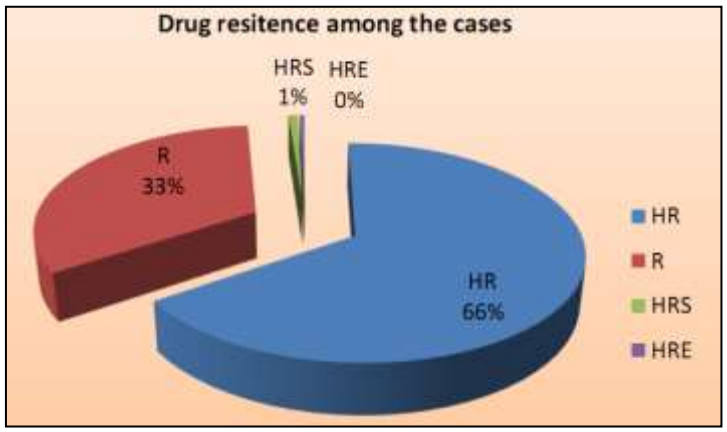

Fig-1: Drug resistance among the cases

.

Out of 244 patients, 60 (24.6%) patients had documented h/o contact with TB patients, of which 53 (88.3%) patients had h/o contact with PTB patients, whereas 7 (11.7%) patients had h/o contact with MDR TB patients. (91.8%) patients had bilateral lung disease, while 20 (8.2%) patients had unilateral lung disease.15 (6.2%) patients had minimal lung disease, 95 (38.9%) patients had moderately advanced lung disease and 134 (54.9%) patients had far advanced lung disease.

On chest radiograph out of 244 patients, 209 (85.7%) patients had cavitatory lung disease, whereas rest had non cavitatory lung disease. Co-morbidities were present in 148 (60.7%) patients. Most common co-morbid condition was COPD present in 104 (42.62%) cases which was mostly smoking related, followed by occupational lung disease (probably silicosis) in 26 (10.65%) cases, Diabetes mellitus in 11 (4.5%) cases, Hepatic disorder in 10 (4.1%) cases, Corpulmonale in 6 (2.5%) cases, HIV infection was present in 6 (2.5%) cases and 3 (1.2%) cases are HbS Ag positive, in 5 (2.0%) cases neurological disorders were present.

DISCUSSION:

The present study was observational study done in Department of Respiratory Medicine in Jawaharlal Nehru Medical College Ajmer, Rajasthan. Most of the patients 231 (94.67%) were from three districts namely Ajmer, Nagaur and Bhilwara. The Ajmer district comprises highest number of patients (n=103, 42.2%). Dhingra *et al.;* [9] (2002-04) also did not find any significant association between geographical distribution of patients and their treatment outcomes.

Among 244 registered patients, 195 (79.92%) were males and mean age of patients was 37.9 years (15-75 yrs.). Mean age of males and females were 38.7 and 34.7 years respectively. In our study population, 182 (74.6%) patients were in reproductive and economically productive age group of 16-45 years. Similar to previous studies, the majority of our cases were males [12, 13].

In our study, to evaluate socio economic status, we used revised Kuppuswamy's Socio-Economic Status Scale. Out of 244 patients, majority 86.88% were from lower and upper lower socioeconomic classes. In our study only 106 (43.44%) patients were literate, out of them 73 (68.86 %) patients educated up to primary school. In case-series study at Nepal by Pant *et al.;* [14] they observed that about 87.0% of the patients (27 out of 31) were belonged to lower socioeconomic and about 77.0% (24 out of 31) of the patients were illiterate. On the contrary the European meta-analysis found no association between low socioeconomic class, literacy and MDR TB by Nirmalya[15]. In the present study 39% had no formal education, 56.1% were employed and 19.5% were unemployed (excluding students).

The association between TB and poverty had been known for centuries, and this also applies to MDR-TB. A case-control study by Barroso *et al.;* [16] suggested a significant inverse association between MDR TB and family income. Tuberculosis affects all groups of people, especially those from lower socioeconomic background. Poverty could be a major predisposing factor, ranging in them from poor overall hygiene, poor living conditions, poor nutrition and immune status. Furthermore, treatment interruptions or defaults were found to be more common among poor families due to job seeking, travelling expenses, loss of work days due to travel for drug, are among other reasons. Propensity of simple tuberculosis developing into MDR TB could have a strong association with poverty. Illiteracy affects patient's knowledge about tuberculosis and its treatment.

Most of the patients in our study were from rural areas (192, 78.7%). In a study by Kliiman *et al.;* [17] (2003-05), 61.7% patients were from urban areas and 38.3 % patients were from rural areas. In our study 145

(59.42%) patients were having addiction habits like Smoking, Alcoholism, Tobacco chewing and Opium intake, while 99 (40.57%) patients had no history of addiction. Ebru *et al.;* [18] (1998-2006) in his study had 27 (42.1%) smoker patients while 37 (57.8%) were non smokers. In our study 57 (23.4%) patients were having history of smoking alone. In study by T.H. Holtz *et al.;* [19], 107 (64.0%) patients were alcohol addict while rest were not.

Alcoholism may contribute to the default behavior and negligence towards anti-tuberculosis medication of patients and therefore may have a negative impact on treatment outcome for tuberculosis. Bhatt G [20] showed around 57% of MDR TB patients were addicted to tobacco and/or alcohol.

In our study, out of 244 patients, 225 patients were married where as radiological improvement was found in 67.0% and 66.7% married and unmarried patients respectively. Thus we observed that there was slightly better outcome in unmarried patients, however this difference was not statistically significant (p value - 0.38, non significant).

In our study, out of 244 patients, 81 (33.2%) patients were Rifampicin mono resistant, 160 (65.6%) patients was HR resistant, 1 (0.4%) patient were resistant to HRE, and 2 (0.8%) patients were resistant to SHR. In our study one patient having drug resistance pattern of HRE and two patients having pattern of drug resistance as SHR were diagnosed by DST results on Conventional Lowenstein Jensen solid media, whereas 241 patients, having resistance to Rifampicin (n=81) and HR (n=160) were diagnosed by Molecular LPA.

DrNirmalya Manna [15] 53.7% patients were found to be resistant to Rifampicin only, 46.3% to both Rifampicin and Isoniazid. In study by Ebru *et al.;* [18] (1998-2006), 18 (28.1%) patients were resistant to HR while resistance to HRE was observed in 11 (17.2%) patients, SHR resistance in 11 (17.2%) patients and HERS resistance in 24 (37.5%) patients. A retrospective analysis of various randomized clinical trials conducted by TRC Chennai with various Rifampicin containing regimens in the initial intensive phase, and with or without Rifampicin in the continuation phase, revealed an overall emergence of resistance to Rifampicin in only 2.0% of patients, despite a high level (18.0%) of initial resistance to Isoniazid, either alone or in combination with other anti-TB drugs. It is to be noted that Rifampicin resistance is quite uncommon without Isoniazid resistance. The great majority of DST results with Rifampicin resistance will also be resistant to Isoniazid, i.e. MDR TB. Therefore RNTCP has taken the programmatic decision that patients, who have any Rifampicin resistance, should be managed as if they are an MDR TB case [21]. Therefore it seems that patients with R resistance may have H resistance also that was not detected by LPA thus R mono resistance may theoretically be same as HR resistance.

Out of 218 (89.3%) patients were under weight i.e. BMI < 18.5 and only 26 (10.7%) patients were in normal range of BMI (18.5 - 24.99. In study by H.R. Kim *et al.;* [54] (1996-2005), they also failed to find any association between initial BMI and outcome (p value = 0.14). Mean BMI in successful treatment group (n=132, 62.5%) was 20.1 while in treatment failure group (n=65, 30.0%) it was 19.1. However nutritional supplements and high protein diet should definitely be considered for MDR TB patients who are under weight (BMI < 18.5). Poulomi Mukherjee [22] Observed mean body mass index (BMI) was 18.5 ± 4.025 kg/m2, range 12 – 31 kg/m2).103 patients (59.88%) were undernourished with BMI less than18.5 kg/m2

In our study Co-morbidities were present in 148 (60.7%) patients. Most common co-morbid condition was COPD present in 104 (42.62%) cases which was mostly smoking related, followed by occupational lung disease (probably silicosis) in 26 (10.65%) cases, Diabetes mellitus in 11 (4.5%) cases, Hepatic disorder in 10 (4.1%) cases, Corpulmonale in 6 (2.5%) cases, HIV infection was present in 6 (2.5%) cases and 3 (1.2%) cases are HBsAg positive, in 5 (2.0%) cases neurological disorders were present. Study by Barroso *et al.;*[16] found COPD in 12 (9%) MDR TB patients and observed that COPD did not increase risk for MDR TB. In our study smoking related co morbid condition may have a role in causing MDR TB which should be further studied by properly designed trials. Study by Barroso *et al.;* [16] found diabetes mellitus in 11 (8.39%) MDR TB patients and observed no co-relation between MDR TB treatment outcome and DM similar to our study. Joseph *et al.;* [21] (2006-07) found that response of diabetic patients was equally good as those without diabetes similar to our study.

Poulomi Mukherjee *et al.*[22]*;* found Chronic obstructive pulmonary disease (COPD) was the commonest comorbidity (17.44%) among the study group followed by Diabetes Mellitus (15.69%) and hypertension (2.32%). Five patients (2.90%) were HIV positive though HIV status was not checked in 15(8.72%) cases.

In our study out of 244 patients, 224 (91.8%) patients had bilateral lung involvement, whereas 20 (8.2%) patients had unilateral lung involvement, along with it, 209 (85.7%) patients had cavitatory lung disease and 35 (14.3%) patients had non cavitatory lung disease, initially at the time of initiation of treatment. Similar rates of cavitation was observed by Zahirifard *et al.;* [23] (80%), Dhingra *et al.;* [9] (81%) from India and M. Rodriguez *et al.;* [24] (78.2%). The reason for varying

frequency of type of lesions may be due to sample size, inter and intra-observer variation and also the nature of the study whether prospective or retrospective.

Of these patients, 130 (58.04%) had bilateral far advanced disease, 89 (39.7%) patients had bilateral moderately advanced disease and 5 (2.2%) patients had bilateral minimal lung disease. Of patients having unilateral lung involvement, 4 (20.0%) patients had unilateral far advanced disease, 6 (30.0%) patients had unilateral moderately advanced disease and 10 (50.0%) patients had unilateral minimal lung disease. Dhingra *et al.;* [9] from India observed more patients (44.44%) with far advance disease similar to the present study.

CONCLUSION:

MDR is strongly affecting all the strategies implied by the government for the prevention and control of tuberculosis. Effective development of data pool for MDR cases is the urgent necessity to combat this creeping malady effectively. This study was an attempt to conform the before mentioned approach and it also warrants and instigates other researcher to do some qualitative research to find out other factors associated with MDR cases more candidly with exorbitant external validity.

REFERENCES:

1. Goble M, Iseman MD, Madsen LA, Waite D, Ackerson L, Horsburgh Jr CR; Treatment Of 171 Patients With Pulmonary Tuberculosis Resistant To Isoniazid And Rifampicin. N Engl J Med 1993; 328: 527-32.
2. Mahmoud AMD, Michael D, Iseman MD; Pitfalls in the Care of Patients with Tuberculosis; Common Errors and Their Association with the Acquisition of Drug Resistance. AMA 1993; 270: 65-8.
3. Narita M, Alonso P, Lauzardo M, Hollender ES, Pitchenik AE, Ashkin D; Treatment experience of multi drug-resistant tuberculosis in Florida, 1994-97. Chest 2001; 120: 343-8.
4. Dheda K, Shean K, Zumla A, Badri M, Streicher EM, Page-Shipp L *et al.;* Early treatment outcomes and HIV status of patients with extensively drug-resistant tuberculosis in South Africa: a retrospective cohort study. Lancet 2010; 375(9728): 1798-1807.
5. Who Global Tuberculosis Report, 2013.
6. National Scale-up Plan for the Programmatic Management of Drug Resistant Tuberculosis (PMDT) 2011–2012. Directorate General of Health Services, Central TB Division, Ministry of Health and Family Welfare.
7. World Health Organization. Global tuberculosis control: WHO report 2012? Geneva, Switzerland; WHO 2012.
8. Guidelines for the programmatic management of drug resistant TB (2006) WHO, Geneva.
9. Dhingra VK, Rajpal S, Anshu Mittal, Hanif M; Outcome of multi-drug resistant tuberculosis cases treated by individualized regimens at a tertiary level clinic; Indian J Tuberc 2008; 55:15-21.
10. Seaworth BJ; Multidrug-resistant tuberculosis. Infect Dis Clin North Am 2002; 16: 73-105.
11. Fisher M; Diagnosis of MDR-TB: a developing world problem on a developed world budget. Expert Rev MolDiagn 2002; 2: 151-9.\
12. Yew WW, Chan CK, Chau CH, Tam CM, Leung CC, Wong PC, Lee J; Outcomes of patients with multidrug-resistant pulmonary tuberculosis treated with ofloxacin/levofloxacin – containing regimens. Chest 2000; 117: 744-751.
13. Telzak EE, Sepkowitz K, Alpert P, Mannheimer S, Medard F, el-Sadr W, *et al.;* Multidrug-resistant tuberculosis in patients without HIV infection. New Engl J Med 1995; 333: 907-911.
14. Pant R, Pandey KR, Joshi M, Sharma S, Pandey T, Pandey S; Risk Factor Assessment of Multidrug-Resistant Tuberculosis: J Nepal Health Res Counc 2009; 7 (15) : 89-92.
15. Manna N , Giri K, Mundle M; Drug resistance pattern, related socio- demographic factors and preventive practices among MDR-TB patients: An experience from a tertiary care setting. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) 2014; 13 (9):16-21.
16. Barroso EC, Salani Mota RM, Oliveira Santos RO, Oliveira Sousa AL, Brasileiro Barroso J, Nobre Rodrigues JL; Risk factors for acquired multidrug-resistant tuberculosis. J Pneumol 2003; 29: 89–97.
17. Kliiman K, Altraja A; Predictors of poor treatment outcomes in multi and extensively drug resistant pulmonary TB. Eur Respir J 2009; 33: 1085-1094.
18. Ebru Unsal, Mujgan Guler, Ruhsar Ofluoglu, Nermin Capan, Filiz Cimen; Factors associated with treatment outcome in 64 HIV negative patients with MDR TB. J Thorac Dis 2013; 5 (4): 435-439.
19. Holtz TH, Sternberg M, Kammerer S, Laserson KF, Riekstina V, Zarovska E, *et al.;* Time to Sputum Culture Conversion in Multidrug Resistant Tuberculosis: Predictors and Relationship to Treatment Outcome. Ann Intern Med.2006; 144(9) : 650-659.
20. Bhatt G, Vyas S, Trivedi K; An epidemiological study of multidrug resistant tuberculosis cases registered under RNTCP of Ahmadabad city. Indian J Tuberc 2012; 59: 18-27.
21. Revised National Tuberculosis Control Programme: Guidelines on Programmatic Management of Drug Resistant TB (PMDT) in India (March 2012). Central TB Division, Director General of Health Services, Ministry of Health and Family Welfare, New Delhi, Government of India. 2012
22. Mukherjee P, Karmakar PR, Basu R, Lahiri SK; Sociodemographic and clinical profile of multi drug resistant tuberculosis patients: a study at drug

resistant tuberculosis centers of Kolkata. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) 2015; 14(8): 52-58

23. Zahirifard S, Amiri MV, Bakhshayesh Kara M, Mirsaeid SM, Ehsanpour A, Masjedi MR; The Radiological Spectrum of Pulmonary Multidrug-Resistant Tuberculosis In HIV-Negative Patients: Iran. 162 J. Radiol, December 2003.
24. Rodriguez M, Monedero I, Caminero JA, Encarnación M, Dominguez Y, Acosta I *et al.;* Successful management of multidrug-resistant tuberculosis under programme conditions in the Dominican Republic; Int J Tuberc Lung Dis 2013; 17 (4):520-525.