

Research Article

Determination of Risk Factors among Multi-Drug Resistant Tuberculosis Patients

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Abstract |

Background: Multi-drug resistant tuberculosis is a type of tuberculosis which is caused by a strain of Mycobacterium tuberculosis complex with resistance to at least one drug that might be isoniazid or rifampicin with or without resistance to any other drug of first-line anti-tuberculosis group. Multiple factors have been identified which lead to multi drug resistance response in tuberculosis.

Objective: To determine risk factors among patients of multi-drug resistant Tuberculosis at public sector health facilities in Lahore.

Methods: Cross sectional study was conducted in outpatient department of chest medicine Public Sector Health Facilities Lahore, Pakistan from 1st January 2017 to 30th June 2017 after obtaining informed consent from Patients of multi drug resistant Tuberculosis in both sexes of age more than 18 years. After simple random sampling 485 patients coming from different cities of whole Punjab were included in this study. The data were entered and interpreted as frequency and percentage distribution. The data were analyzed by Statistical Package for Social Sciences (SPSS) version 22.

Results: Among 485 patients of multi-drug resistant Tuberculosis there were 248 males and 237 females. 126 (25.98%) patients had known contact with multi-drug resistant tuberculosis patients. 39(8.04%) had poor Tuberculosis (TB) program performing facility. 48(9.90%) had treatment failure and presented with different co-morbidities. Only 2 male cases (0.41%) had human immunodeficiency virus and 39(8.04%) had diabetes Mellitus. 27(5.57%) cases had prior course of therapy included rifampicin throughout treatment and poor compliance of treatment was seen in 73(15.05%) cases. Smoking history and addiction was observed among 29(5.98%) and 15(3.09%) cases.

Conclusion: The risk factors for TB and multi drug resistant Tuberculosis were not same except the history of contact, inadequate treatment and treatment failure. Addiction and human immunodeficiency virus in multi-drug resistant tuberculosis were also uncommon factors. Addiction / consumption of alcohol was common in minorities specially Christians.

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Keywords | Multi-drug resistant tuberculosis, Mycobacterium, Human immunodeficiency virus/ auto immune deficiency syndrome, Malabsorption

Introduction

Multi-drug resistant tuberculosis (TB) is a type of tuberculosis which is caused by a strain of *Mycobacterium tuberculosis* complex with resistance to at least one drug that might be isoniazid or rifampicin with or without resistance to any other drug of first line anti-tuberculosis group. Multiple factors have been identified which lead to multi drug resistance response in TB.⁽¹⁾

Multi drug resistant TB cases have been reported in all countries where survey is done.⁽²⁾ Multi drug resistant tuberculosis is commonly developed in the course of tuberculosis treatment.⁽³⁾ The cases are most commonly observed where doctors are doing inappropriate treatment or patient failing to complete their treatment or missing doses, because multi drug resistant TB is contagious disease, if the patients with active tuberculosis caused by multi drug resistance are coughing, they can transmit the disease to others². Small epidemics occur more readily in population with a weak immune system.⁽⁴⁾ It is less common that outbreaks can occur in more immunocompromised people.⁽⁵⁾ According to 2013 statistics 37% multi drug resistant tuberculosis cases are new. In previously treated tuberculosis patients' levels are much higher. According to World Health Organization (WHO) in 2011 there was about 0.5 million new cases of multi drug resistant TB globally. Only 6% cases accrued in China, India, Brazil, South Africa and Russian Federation⁶. The rise of Multi-Drug Resistant Tuberculosis (MDR-TB) in Maldev is due to crumbling health system.⁽⁵⁾ A very hot region for drug resistant TB "was noted to be Mexico-initial state border in 2013, despite small number of cases⁷.

Pakistan has been ranked 5th in the 22 high tuberculosis burden countries and 4th among the countries where multi-drug resistant TB has become a serious challenge for the clinicians. Pakistan has developed multi drug resistance in approximately 2 - 3.2 % of newly diagnosed TB case and 35% patients are of previously treatment.⁽⁸⁾

There are multiple factors those make people susceptible to TB infections. Human Immunodeficiency Virus (HIV)/ Acquired Immune Deficiency Syndrome (AIDS) is the most important and common risk factor in the world; 13% of TB patients

are infected by the HIV.⁽⁹⁾ This is the major issue in areas of Africa (sub Saharan), The rates of HIV are very high in these areas.^(10,11) the HIV people those are commonly infected with TB, there is active disease during their lifetimes in 5-10% cases;⁽³⁾ whereas, 30% of HIV patients develop the active disease.⁽³⁾ Tuberculosis is one of the major diseases of poverty linked to both overcrowding and malnutrition.⁽¹²⁾ High population risk thus include: the people who take drugs through injections, residents of locales where there is gathering of vulnerable people (e.g. homeless shelters and prisons), resource-poor people medically and underprivileged, ethnic minorities with high risk, health-care providers serving these patients and children those have close contact with high-risk people.⁽¹³⁾ One of the significant risk factors is chronic lung disease. There is increase of the risk about 30-fold due to silicosis,⁽¹⁴⁾ the smokers have double the risk of TB as compared to non-smokers-those.⁽¹⁵⁾ There is also increase of the risk of developing TB in other disease states. There is threefold increase of Tuberculosis due to alcoholism⁹ and diabetes mellitus⁽¹⁶⁾ HIV/AIDS people are 20 to 30 times more to develop active Tuberculosis. The patients suffering from other diseases those impair the immune system are on greater risk of this disease.

In 1943 when first antibiotic management for TB was started, resistance was developed to the standard drugs after genetic changes by some strains of TB bacteria¹⁷. There is acceleration of the process when there is an inadequate or incorrect medication. As a result of the improper and irregular treatment, there is development of multi drug resistant TB,^(5,6) Second line drugs (Amino-glycosides, Fluoroquinolones etc.), are generally expensive and more toxic with least efficacy.⁽¹⁸⁾ If these second line drugs are taken or prescribed incorrectly, resistance may be developed which can lead to Extensively Drug Resistant TB (XDR-TB).

There is presence of resistant strain of TB in the population so there is transmission of multi drug resistant TB from infected person to healthy person and there is development of new case of multi drug resistant TB in a previously untreated case. Such a type of cases is called primary multi drug resistant TB and cause approximately 75% of cases.⁽¹⁹⁾ When a patient with a non-resistant strain of tuberculosis is treated inadequately, develops acquired multi drug

resistant, causing antibiotic resistance in antibiotics in the tuberculosis bacteria infecting them. These patients can infect others with multi drug resistant tuberculosis.⁽¹⁸⁾ Multi drug resistant TB cases are managed with second line drugs; those might be four or more anti-TB drugs for the minimum period of six months if resistance in rifampicin has been found in concerned strain of TB that has infected the patients.⁽²⁰⁾ In ideal condition cure rates of multi drug resistant TB can approach 70%.⁽²⁰⁾

Risk factors for multi-drug resistant TB include failure of treatment, proven incarceration and failure to response to standard tuberculosis management, HIV/AIDS infection and relapse after standards management, in addition to a known exposure to a patient with multi drug resistant TB. The sensitivity testing should be basis for management of multi drug resistant TB without the infection. It is not possible to treat such patients. Keep delaying the result of laboratory sensitivity testing when testing a patient with multi drug resistant tuberculosis, treatment with SHREZ (streptomycin, isoniazid, rifampicin, ethambutol and pyrazinamide)+moxifloxacin and cycloserine should be started. This is obvious that old treatment with a drug for the period of one month with minimum efficacy is indicating susceptibility,⁽²¹⁾ that is why the previous history of treatment of every patient is essential. It is generally understood that resistance with one drug is meant resistance to all drugs within that class except rifabutin. Resistance to rifampicin is not meant rifabutin resistance and there should be laboratory test. One drug within each drug class should be used. The clinician should think that high load Isoniazid (INH) resistance be probed for if it is not easy to find out five drugs to treat. High dose INH can be given as part of the treatment if the strain has low level of INH resistance. When counting drugs for treatment of TB, pyrazinamide (PZA) is counted as zero, it means adding PZA to regimen for four drugs; one drug must be chosen to make five. Use of more than one injectable is not possible due to addition of toxic effects. If necessary then aminoglycosides can be started for the period of three months. If other fluoroquinolone are available then ciprofloxacin should not be used in the management of tuberculosis²². There should be isolation of patients with multi-drug resistance in negative pressure rooms. Immunosuppressed patients should

not be kept in wards where multi drug resistant TB patients are admitted, It is crucial to monitor carefully the complications with treatment of multi drug resistant tuberculosis because some consultants insist for admission of these patients. There is insistence of some physicians that there should be isolation of these patients till their sputum smear becomes negative. It is impossible to help these patients in hospitals for a long time so clinical judgment of the physician, treating these patients is the final decision. The consultant should use therapeutic drugs, monitor not to have toxic effects and for compliance. Some supplements can be used as adjuncts in the management of TB but those should not be counted in drugs for management of multi drug resistant TB. Addition of arginine or vitamin D or both may be beneficial but this will be counted as zero.⁽²³⁾

A study conducted by National Referral Institute for tuberculosis and Lung diseases Tehran, Iran from 2002 to 2005 showed that underlying conditions like diabetes mellitus also could lead to MDR tuberculosis. In this study, relative analysis of the nationality of multidrug resistant TB patients compared to non-MDR tuberculosis cases (p -value < .002), revealed that out of 78 afghan patients, 22 (46.8%) consisted of the multidrug resistant TB category whereas 56(23.9%) belonged to the non-multi drug resistant TB category.

Multi-drug resistant TB therefore was found to be more prevalent among afghan patients than the other nationalities. Non-multi-drug resistant tuberculosis with 177 cases (75.6%) was more common than multi-drug resistant TB cases (24 cases-51.1%) among a total of Iranian 201 cases. Also, 2.1% of the data belonged to Bangladesh. Positive previous history of anti-TB medication was higher in multi-drug resistant tuberculosis group as compared to non-multi drug resistant TB controls. (p -value < .001); A positive previous history of anti-TB medicines was reported among 95.8% of multi-drug resistant TB cases. Whereas non multidrug resistant group included 23.10% cases. All multi-drug resistant TB patients (95.7%) except two had positive sputum smears for Acid Fast Bacilli (AFB) whereas 81.2% of non-multi-drug resistant tuberculosis patients had positive smears. Dyspnea was another significant variable. It was commonly found among multi-drug resistant TB cases (85.1%) than in non-multi drug

resistant tuberculosis patients (68.4%).⁽²⁴⁾ According to a study conducted in Pakistan, a patient having renal failure and tuber-culosis could also develop multi-drug resistant TB. Another study conducted from 2006 to 2008 in Shanghai, China, showed that inclination towards alcoholism and smoking could lead to multi-drug resistant TB. In Shanghai, China, anti-TB drug resistance surveillance study conducted during 2000-2006 showed that another risk factor for multi-drug resistant TB was the positivity of smears even after having anti-TB treatment for 3 months.²⁵ A study conducted in Denver, Colorado between years 1973 and 1983 showed that inadequate anti-TB treatment regimens in 47 cases (35%) out of 134 developed multi drug resistant TB.⁽²⁶⁾ A case-control study was conducted by Ministry Of Health and Social Services, Namibia in 9 cities between January 1, 2007 and March 31, 2009. This study revealed that poorly handled previously hospitalized tuberculosis cases could also develop multi drug resistant TB (Odds Ratio 1.9, 95% CI 1.1–3.5). Total multi-drug resistant TB cases in this study were 117 and controls 271.⁽²⁶⁾

A study conducted in public sector health facilities Lahore, Pakistan showed that multi drug resistant tuberculosis developed in 31 (62%) patients (11 males and 20 females were included) who had completion of re-treatment regimen in the past and were still sputum smear was positive for acid fast bacilli.⁽²⁷⁾ A multi-center, prospective study was conducted in 1993 by the National Institute of Allergy and Infectious Diseases, New York, USA under the auspices of the community program for clinical research on AIDS (CPCRA) and the AIDS clinical trials group (ACTG). The purpose of this study was to analyze the demographic, behavioral, geographic, clinical and risk factors related with the occurrence of multi drug resistant tuberculosis in HIV-infected patients. The study revealed that previous anti-tuberculosis treatment especially in HIV-infected patients with TB was also a major risk factor for developing multi-drug resistant TB (Odd Ratio = 4.4, $p < 0.02$).⁽²⁸⁾

A study conducted in Thailand in 2001 showed that primary multi-drug resistant tuberculosis occurred in 8.2% out of 377 HIV-positive patients.⁽²⁹⁾ According to a study in United Kingdom in 2013, it was observed that multi-drug resistant tuberculosis was more common in some groups, such as the former prison

inmates.⁽³⁰⁾ A study was conducted between 1996 and 2001 on pregnant women with confirmed multi-drug resistant TB. In this study, it was found out that 3 out of 5 cases with multidrug resistant TB in pregnant women were related with HIV-1. There was termination of pregnancy in one women and there was pre-term labor in one woman. There was growth restriction in two neonates.⁽³¹⁾

As for Pakistan is concerned the emerging of multi-drug resistant (MDR) strains of TB became an important challenge for the healthcare sector in the country. Multi-drug resistant TB strains are resistant to a number of first lines anti TB drugs including "at least isoniazid and rifampicin."⁽³²⁾ Pakistan is ranked the top ten countries in the world with regards to the disease burden of TB and the high incidence and prevalence of the disease in this country, has been related to several factors such as low nutritional level, poverty, patient noncompliance, low awareness and suboptimal healthcare infrastructure.^(33,34)

In Pakistan the rates of multi-drug resistance tuberculosis vary from 2.3% to an alarming 17.9% in individuals those have been previously treated for the disease.⁽³⁶⁾ Recently there is documentation of several studies showing overall trends of multi-drug resistant tuberculosis in Pakistan. A study has given results, an almost. There is constant increase of number of multi-drug resistant cases of TB as resulted by one study from 1990 - 2007 with isolation of more than 15,000 cases during that period.⁽³⁵⁾

Keeping in view all studies, as cases of multi-drug resistant TB are increasing in Pakistan, there was dire need to probe the factors causing multi-drug resistant tuberculosis in this country.

Methods

Cross sectional study was conducted in outpatient department of Chest Medicine Public Sector Health Facilities Lahore from 1st January 2017 to 30th April 2017 after taking informed consent from patients of multi-drug resistant tuberculosis of both sexes of age more than 18 years. After simple random sampling 485 patients coming from whole Punjab were included in this study. Data were collected on a specified questionnaire and required information after interviewing the patients was recorded. The data were entered and interpreted as frequency and

percentage distribution. Only registered patients of multi drug resistant Tuberculosis were included in this study. The data were analyzed by Statistical Package for Social Sciences (SPSS) version 22.

Results

Among 485 patients of multidrug resistant tuberculosis, there were 237 males and 248 females. There were 126 (25.98%) cases who had known contact with patients of MDR TB. A total of 39(8.04%) cases had poor TB program performing facility and poor drug quality system. There were 48(9.90%) cases those had treatment failure and presented with different co-morbidities like (malabsorption, chronic diarrhea). Only 2 cases (0.41%) had HIV history and 39(8.04%) cases had diabetes mellitus. There were 27(5.57%) cases those had prior course of therapy included rifampicin throughout treatment and poor compliance of treatment was seen in 73(15.05%) cases. Smoking history and addiction was observed among 29(5.98%) and 15(3.09%) cases.

There were 126 (25.98%) who had known contact with MDR TB patient. A total of 39(8.04%) had poor TB program performing facility and poor drug quality system. There were 48(9.90%) cases that had treatment failure and presented with different co-morbidities like (malabsorption, chronic diarrhea). Only 2 cases (0.41%) had HIV history and 39(8.04%) had DM. There were 27(5.57%) cases who had prior course of therapy included rifampicin throughout treatment and poor compliance of treatment was seen in 73(15.05%) of the cases. Smoking history and

Table 1: Risk Factors of Multi Drug Resistant Tuberculosis

Sr. No	Risk factors of Multi Drug Resistant Tuberculosis	No. of Patients	Percentage
1-	Known contact with mdr-tb patient	126	25.98
2-	Poor tb program performing physility	39	8.04
3-	Poor drug quality-poor drug quality	39	8.04
4-	Treatment failure	48	9.90
5-	Patient with co-morbidity conditions (malabsorbtion, ch.diarrhea)	48	9.90
6-	Patient having hiv	02	0.41
7-	Patient having type 2 diabetes mellitus	39	8.04
8-	Patient whose prior course of therapy included rifampicin throughout treatment	27	5.57
9	Poor compliance to treatment	73	15.05
10-	Smoking	29	5.98
11-	Addiction (Alcohol consumption)	15	3.09

alcohol consumption was seen 29(5.98%) and 15(3.09%) of the case

According to known contact with MDR-TB there were 64 male and 62 females while 173 male and 186 females did not have known contact with MDR-TB, there was significant association between gender and known contact with MDR-TB, p-value > 0.05. There were 18 male and 21 female cases who had poor TB performing facilities while 219 and 227 male and females did not have poor TB performing facility, there was no association of poor TB performing facility with gender, p-value > 0.05. There were 21

Table 2: Association between Gender, MDR-TB contact, Poor Facility, Drug Quality and Treatment Failure

		Known Contact with MDR-TB		Poor TB Performing Facility		Poor Drug Quality		Treatment Failure	
		Yes	No	Yes	No	Yes	No	Yes	No
Gender	Male	64(47.61%)	173	18(46.15%)	219	21(53.85%)	216	26(54.17%)	211
	Female	62(49.20%)	186	21(53.85%)	227	18(46.15%)	230	22(45.83%)	226
	p-value	0.615		0.724		0.516		0.439	
Age group (years)	18-24	11	474	04	481	04	481	06	479
	25-34	22	463	09	476	09	476	08	477
	35-44	21	464	09	476	09	476	10	475
	45-54	30	455	11	474	11	474	11	474
	55-64	30	455	04	481	04	481	09	476
	>64	12	473	02	483	02	483	04	481
	p-value	0.004*		0.069		0.069		0.504	

male and 18 females who had poor drug quality while 216 male and 230 female cases that did not have poor drug quality with no statistical association, $p\text{-value} > 0.05$. In this study there were 26 male and 22 female who had treatment failure and 211 male and 226 females did not have treatment failure with no significant association, $p\text{-value} > 0.05$. According age distribution we found significant association of known contact with MDR with advanced age group i.e. 11 cases were 18-24 years old, 22 cases were 25-34 years old, 21 cases were 35-44 old, 30 cases were

45-54 and 55-64 years old each and 12 cases were > 64 years of age, $p\text{-value} < 0.05$. Moreover there was no significant association between age groups and Poor TB performing facility, Poor drug quality and Treatment failure, $p\text{-value} > 0.05$. (Table 2)

Table 3: Association Between Gender & Co-Morbidly Condition HIV/AIDS and Type 2 Diabetes Mellitus.

		Co -Morbidly Conditions		HIV/AIDS		T2 DM	
		Yes	No	Yes	No	Yes	No
Gender	Male	20 (41.66 %)	217	02(0.41%)	235	16(46.03%)	221
	Female	28 (58.33%)	220	0	248	23(58.97%)	225
	p-value	0.293		0.147		0.307	
Age group (years)	18-24	06	479	01	484	03	482
	25-34	06	479	0	0	06	479
	35-44	11	474	01	484	09	476
	45-54	14	471	0	0	11	474
	55-64	07	478	0	0	06	479
	>64	04	481	0	0	04	481
	p-value	0.113		1		0.214	

There were 20 male and 28 female cases who had comorbid conditions, only 2 male cases were HIV/AIDS positive while 16 male and 23 females cases had T2 DM. We found no significant association between gender and co-morbidly conditions, HIV/AIDS and T2 DM, $p\text{-value} > 0.05$. Moreover there was no significant association between age groups and co-morbidly conditions, HIV/AIDS and T2 DM, $p\text{-value} > 0.05$. (Table 3)

There were 10 male and 17 female cases who had prior course of therapy included rifampicin, 26 male and 47 female cases had poor compliance to treatment, 21 male and 8 female cases were smokers while 13 male and 2 female cases had addiction/ alcohol consumption. A significant association was found between prior gender and poor compliance to treatment, Smoking and addiction/Alcohol consumption, $p\text{-value} < 0.05$. (Table 4) While these variables did not have any significant association with age

groups, $p\text{-value} > 0.05$ (Table 4)

Among 126 patients there were 64(47.61%) male and 62(49.2%) female cases who had known contact with TB. No significant association was seen between gender and age groups, $p\text{-value} > 0.05$. There were 18(46.15%) male and 21(53.85%) female cases among 39 patients had poor TB program performing facility. No significant association was seen between gender and age groups, $p\text{-value} > 0.05$.

Among 39 patients there were 21(53.85%) male and 18(46.15%) female cases who reported poor drug quality. No significant association was seen between gender and age groups, $p\text{-value} > 0.05$. There were 26(54.17 %) male and 22(45.83%) female cases who had treatment failure among 48 patients. No significant association was seen between gender and age groups, $p\text{-value} > 0.05$ among 48 patients there were 20(41.66%) male and 28(58.33%) female cases that had co-morbidity conditions. No significant associa-

Table 4: Association Between Gender, Prior Therapy and Poor Compliance to Treatment

		Prior Course of Therapy Included Rifampicin		Poor Compliance to Treatment		Smoking		Addiction/Alcohol Consumption	
		Yes	No	Yes	No	Yes	No	Yes	No
Gender	Male	10(37.03%)	227	26(35.61%)	211	21(72.41%)	216	13(86.63%)	224
	Female	17(62.97%)	231	47(64.39%)	101	08(27.59%)	240	02(13.37%)	246
	p-value	0.206		<0.001**		0.009*		0.003*	
Age group (years)	18-24	02	483	08	477	04	481	01	484
	25-34	08	477	13	472	09	476	06	479
	35-44	07	478	14	471	08	477	04	481
	45-54	06	479	15	470	05	480	02	483
	55-64	02	483	14	471	02	483	02	483
	>64	02	483	09	476	01	484	0	0
	p-value	0.115		0.607		0.059		0.252	

tion was seen between gender and age groups, p -value > 0.05 . There were 16(46.03%) male and 23(58.97%) female cases that had type 2 diabetes mellitus among 39 patients. No significant association was seen between gender and age groups, p -value > 0.05 . Among 27 patients there were 10(37.03%) male and 17(62.97%) female cases who had prior course of therapy included rifampicin throughout treatment. No significant association was seen between gender and age groups, p -value > 0.05 . There were 26(35.61%) male and 47(64.39%) female cases who had poor compliance to treatment among 73 patients. No significant association was seen between gender and age groups, p -value > 0.05 . Among 29 patients there were 21(72.41%) male and 8(27.59%) female cases who were smokers. No significant association was seen between gender and age groups, p -value > 0.05 . There were 13(86.63%) male and 2(13.37%) female cases with addiction (alcohol consumption) among 15 patients. Majority of them were Christians. No significant association was seen between gender and age groups, p -value > 0.05 .

Discussion

For development of resistance in TB due to any drug, there were many factors involved like inadequate chemotherapy, poor treatment, poor drug quality, cavity pulmonary tuberculosis poor adherence to treatment, treatment failure, HIV infection and diabetes mellitus.^(36,37) The most important predictor for the establishment of multi-drug resistant tuberculosis was the previous history of management.⁽¹⁰⁾ A number

of new cases developed due to mismanagement of tuberculosis like using of one drug, in addition to a one drug to a regimen which failed, indirectly failing is found out preexisting resistance, inadequate use of first line anti-tuberculosis drugs. There is development of multi-drug resistant TB after the bioavailability variations of anti-tuberculosis drugs.^(36,37)

When a patient with a non-resistant strain of tuberculosis is treated inadequately, develops acquired multi drug resistant, causing antibiotic resistance in antibiotics in the tuberculosis bacteria infecting them. These patients can infect others with multi drug resistant TB.⁽³⁸⁾

Risk factors for multidrug resistant TB include failure of treatment, proven incarceration and failure to response to standard TB management, HIV/AIDS infection and relapse after standards management, in addition to a known to exposure to a patient with multi drug resistant TB. The sensitivity testing should be basis for management of multi drug resistant tuberculosis without the infection. It is not possible to treat such patients. Keep delaying the result of laboratory sensitivity testing when testing a patient with multi drug resistant TB, treatment with SHREZ (streptomycin, isoniazid, rifampicin, ethambutol and pyrazinamide)+moxifloxacin and cycloserine Should be started. This is obvious that old treatment with a drug for the period of one month with minimum efficacy is indicating susceptibility,⁽³⁹⁾ that is why the previous history of treatment of every patient is

essential. It is generally understood that resistance with one drug is meant resistance to all drugs within that class except rifabutin. Resistance to rifampicin is not meant rifabutin resistance and there should be laboratory test. One drug within each drug class should be used. The clinician should think that high load INH resistance be probed for if it is not easy to find out five drugs to treat. High dose INH can be given as part of the treatment if the strain has low level of INH resistance. When counting drugs for treatment of TB, PZA is counted as zero, it means adding PZA to regimen for four drugs; one drug must be chosen to make five. Use of more than one injectable is not possible due to addition of toxic effects. If necessary then aminoglycosides can be started for the period of three months. If other fluoroquinolone are available then ciprofloxacin should not be used in the management of tuberculosis.⁽⁴⁰⁾

In one study, diabetes mellitus had been there as a comorbid disease in 7.6% patients. In other study 15.69% cases were diabetics. Internationally multi-drug resistant TB cases were from HIV/ AIDS patients, having lower rate of survival as compared to non-infected patients. Due to this reason HIV testing should be done for all patients. There is scanty literature from different parts of the India regarding multi-drug resistant TB cases with HIV. There was report by Data et al that there was seropositivity in 1.95 HIV cases associated with multi-drug resistant TB cases. There was seropositivity of HIV found in 2.90% multi-drug resistant TB cases.⁽⁴¹⁾

In this study there were 25.98% cases who had known contact with multi-drug resistant TB patients. It was observed that positive history of contact was also the major risk factor in multi-drug resistant tuberculosis and it was observed in approximately in 26%. A total of 8.04% had poor TB program performing facility and poor drug quality system. There were 9.90% cases that had treatment failure and presented with different co-morbidities like (malabsorption, chronic diarrhea). Only 0.41% cases had HIV history and 8.04% had Diabetes Mellitus. There were 5.57% cases that had prior course of therapy included rifampicin throughout treatment and poor compliance of treatment was seen in 15.05% of the cases. Smoking history and addiction (alcohol consumption) was observed in 5.98% and 3.09% cases. Addiction / alcohol consumption was common

in minorities specially in Christians.

In this study among 126 patients, there were 50.79% males and 49.21% female cases who had known contact with TB. No significant association was seen between gender and age groups, p-value was > 0.05 . There was 46.15% male cases and 53.85% female cases among 39 cases that had poor TB program performing facility meant that treatment was not according to WHO regimen. No significant association was seen between gender and age groups, p-value > 0.05 . From total of 39 there was 53.85% male and 46.15% female cases who reported poor drug quality or drugs those were under dose. No significant association was seen between gender and age groups, p-value > 0.05 . There were 54.17 % males and 45.83% female cases among 48 cases who had treatment failure or physician's negligence. No significant association was seen between gender and age groups, p-value was > 0.05 .

Conclusion

It was concluded that risk factors like contact with patients of multi-drug resistant TB, poor program facility, poor drug quality, treatment failure, co-morbidly conditions, HIV/AIDS, diabetes mellitus, inclusion of rifampicin throughout the treatment, poor compliance of treatment are common in this study. The HIV was not common in multi-drug resistant TB because transmission of HIV is very uncommon in our population.

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