

## IDENTIFICATION OF DIFFERENT FACTORS LEADING TO THE DEVELOPMENT OF MULTIDRUG RESISTANCE TUBERCULOSIS.

DR. MUHAMMAD TALHA AIZAZ

MBBS,

HOUSE OFFICER, NISHTAR HOSPITAL, MULTAN

DR. SHAWAIZ ABDULLAH,

MBBS

HOUSE OFFICER, NISHTAR HOSPITAL, MULTAN

DR. HUMAYUN BABAR

MBBS

HOUSE OFFICER, NISHTAR HOSPITAL, MULTAN

### ABSTRACT;

**Background;** Despite an overall decreasing incidence and mortality rate for tuberculosis (TB), multidrug resistance tuberculosis (MDR-TB) continues to be a serious threat to the current global tuberculosis control effort. Failure to control MDR-TB may lead to another era with TB being regarded as a fatal disease. **Materials and Method;** One hundred forty one cases confirmed MDR-TB patient by of either gender aged less than 60 years who were newly diagnosed or who were previously diagnosed cases were enrolled in this descriptive study. Demographic, socioeconomic, clinical as well as laboratory data were recorded for each patient by trained data collector. The data was collected through pre-tested close ended questionnaire. Drug resistant cases was labeled according to sputum culture Sensitivity report and GeneXpert for MTB and were assessed for different factors for MDR. **Results;** Our study comprised of 141 study cases of MDR TB, 71 (50.4%) were male patients and 70 (49.6 %) were female patients. Mean age of our study cases was  $39.99 \pm 9.15$  years One hundred and five (74.5%) of our study cases were married while 36 (25.5%) were unmarried. Majority of our study cases were less educated as 47 (33.3%) were illiterate and 78 (55.3%) were having primary level of education. Majority of our study cases were living in slum areas and were having poor socioeconomic status as 77 (54.6%) were having their family income less than Rs. 10, 000 per month. Previous history of TB was present in 99 (70.2 %) of our study cases. Good compliance with the treatment was present in only 28 (19.9%) of our study cases. History of close contact with TB patient was reported by 92 (65.2%) of our study cases, 20 (14.2%) were defaulters and 42 (29.8%) presented with treatment failure. History of HIV infection was zero in our study. **Conclusion;** Previous history of Tuberculosis with poor compliance with drug therapy was the major risk factor for the development of MDR TB in our study. History of close contact with TB patients was another important risk factor in the development of MDR TB. Other important risk factors were previous history of tuberculosis infection, living in urban slum areas, poor educational status and poor socioeconomic status were more common.

**Keywords;** Multidrug resistance, Tuberculosis, Risk factors.

## INTRODUCTION

Tuberculosis is a major infectious health problem; over two billion people are affected by this disease annually throughout the world. TB represents more than a quarter of world's preventable death<sup>1</sup>. Multi Drug Resistant Tuberculosis (MDR-TB) prevalence in South East Asia is estimated as 2.8% (95% CI, 1.9 to 3.6) among new cases and 18.58% (95% CI, 13.3 to 24.3) among previous treated cases<sup>2</sup>. According to WHO Global TB report 2011, Pakistan ranks 5th among 22 high burden countries in TB and 4th among 27th high Multi Drug Resistant Tuberculosis (MDR-TB) countries, the percentage of Multi Drug Resistant Tuberculosis (MDR-TB) is 3.4 among new tuberculosis cases and 21 among retreated cases. It is realized that there is rising incidence of Drug Resistant Tuberculosis.

Currently Multi Drug Resistant Tuberculosis (MDR-TB) is considered as one of most important threats to TB control effort through the world<sup>3</sup>. According to WHO's fourth global report in Anti-TB drug resistant, there were an estimated 4.8% of all new cases which were diagnosed as Multi Drug Resistant Tuberculosis, greatest numbers of such cases reported from Pakistan, China, India, and Russia<sup>4</sup>. From individual perspective, Treatment failures with first line Rifampicine containing regimens and contact of Multi Drug Resistant Tuberculosis case have highest rates of resistant<sup>5</sup>. Despite a comparatively higher disease prevalence of this disease amounting to 263/100,000 population among its neighboring countries, Pakistan Lacks the updated regional information about the Drug resistant TB<sup>6</sup>. A recently published study indicated Multi Drug Resistant Tuberculosis rate of 1.8% amongst untreated patients presenting to TB clinics within Pakistan<sup>7</sup>.

Multi Drug Resistant Tuberculosis is microbial, clinical and programmatic issue. From microbiological perspective, resistant is caused by a genetic mutation that makes a drug ineffective. Percentages of various risk factors for MDR-TB are

- 1) Previous history of tuberculosis (82.6%)<sup>8</sup>.
- 2) Previous history of treatment of tuberculosis (100%)<sup>9</sup>, out of which 67 % had missed a few weeks drugs during this previous treatment and 13% had been marked as defaulter and 20% had treatment failure .
- 3) Poor compliance (60.9%)<sup>8</sup>.
- 4) History of contact with MDR-TB patients ( 42.6%)<sup>10</sup>.
- 5) HIV (6.2%)<sup>9</sup>.

These factors have contributed to poor patient compliance and future increasing prevalence of Multi-Drug Resistant Tuberculosis (MDR-TB) as well as emergence of Extensive Drug Resistant Tuberculosis (XDR-TB).

## Materials and Method

One hundred forty one cases confirmed MDR-TB patient by Culture and DST and GeneXpert for MTB of either gender aged less than 60 years who were newly diagnosed or who were previously diagnosed cases were enrolled in this descriptive study. Patients who had diabetes, HIV, asthma, incomplete clinical record, malignancies and hypertension were not included in this study. Demographic, socioeconomic, clinical as well as laboratory data were recorded for each patient by trained data collector. The data was collected through pre-tested close ended questionnaire. Drug resistant cases was labeled according to sputum culture Sensitivity report and GeneXpert for MTB. The data was entered in statistical program for social sciences (SPSS) version 18.

## Results;

Our study comprised of 141 study cases of MDR TB who met inclusion and exclusion criteria of this study. Of these 141 study cases, 71 (50.4%) were male patients and 70 (49.6 %) were female patients. Mean age of our study cases was  $39.99 \pm 9.15$  years (with minimum age was 25 years while maximum age was 53 years). Our study results have indicated that majority of our study cases i.e. 78 (55.3%) were less than 40 years of age. One hundred and five (74.5%) of our study cases were married while 36 (25.5%) were unmarried. Majority of our study cases were less educated as 47 (33.3%) were illiterate and 78 (55.3%) were having primary level of education. Majority of our study cases were living in slum areas and were having poor socioeconomic status as 77 (54.6%) were having their family income less than Rs. 10, 000 per month. Previous history of TB was present in 99 (70.2 %) of our study cases. Good compliance with the treatment was present in only 28 (19.9%) of our

study cases. History of close contact with TB patient was reported by 92 (65.2%) of our study cases, 20 (14.2%) were defaulters and 42 (29.8%) presented with treatment failure. History of HIV infection was zero in our study.

**Table No. 1**  
**Stratification of risk factors with regards to gender.**  
**(n=141)**

Risk factors		Gender		P – value
		Male (n=71)	Female (n=70)	
Previous history of TB	Yes	43	56	<b>0.016</b>
	No	28	14	
History of treatment of TB	Yes	28	29	<b>0.865</b>
	No	43	41	
Compliance	Good	28	00	<b>0.000</b>
	Poor	43	70	
Close contacts	Yes	71	21	<b>0.000</b>
	No	00	49	
Defaulters	Yes	02	18	<b>0.000</b>
	No	69	52	
Treatment failure	Yes	28	14	<b>0.016</b>
	No	43	56	

## DISCUSSION;

Multidrug-resistant tuberculosis (MDR-TB), which is defined as TB caused by strains of *Mycobacterium tuberculosis* (MTB) that are resistant to at least isoniazid (INH) and rifampicin (RFP), is a form of TB infection linked with high morbidity and mortality, and it is of great importance to the National TB Control Program (NTP). MDR-TB results from primary infection with resistant bacteria (primary MDR-TB), or it may develop in the course of a patient's treatment (acquired MDR-TB) <sup>11-19</sup>.

Our study comprised of 141 study cases of MDR TB who met inclusion and exclusion criteria of this study. Of these 141 study cases, 71 (50.4%) were male patients and 70 (49.6 %) were female patients. Rifat et al <sup>17</sup> from Bangladesh reported 60 % male predominance in their study, which is bit high proportion than that of our findings. Mulu et al <sup>18</sup> reported 57 % male patients having MDR TB, these findings are close to our study results. Mean age of our study cases was 39.99 ± 9.15 years (with minimum age was 25 years while maximum age was 53 years). Our study results have indicated that majority of our study cases i.e. 78 (55.3%) were less than 40 years of age. Rifat et al <sup>17</sup> from Bangladesh reported 37 years mean age of the patients with MDR TB, which is close to our study results. Mulu et al <sup>18</sup> also reported MDR TB being more common in young patients with ages less than 45 years which is in accordance with our study results. Li et al <sup>11</sup> reported 37.59 years mean age, which are close to that of our study results. One hundred and five (74.5%) of our study cases were married while 36 (25.5%) were unmarried. Mulu et al <sup>18</sup> reported 37 % MDR TB patients were married, these findings are similar to that of our study results. In our study, 66 % of our patients were from Urban areas while a study conducted by Mulu et al <sup>18</sup> reported 74 % patients from Urban areas, these findings of Mulu et al are similar to that of our study results. Similar findings were made by Rifat et al <sup>17</sup>.

Majority of our study cases were less educated as 47 (33.3%) were illiterate and 78 (55.3%) were having primary level of education. Rifat et al <sup>17</sup> from Bangladesh also reported MDR TB being more prevalent in

less educated patients living in slum areas, these findings support our study results. Similar results have been reported by Mulu et al.<sup>18</sup> Majority of our study cases were living in slum areas and were having poor socioeconomic status as 77 (54.6%) were having their family income less than Rs. 10, 000 per month. Rifat et al<sup>17</sup> reported MDR TB was associated with poor socio-economic status which is in accordance with our study results. Wang et al<sup>19</sup> from China reported similar findings of MDR TB being more common in patients having lower socio-economics. Similar results have been reported by Mulu et al<sup>18</sup>.

Previous history of TB was present in 99 (70.2 %) of our study cases. A study conducted by Li et al<sup>11</sup> reported 44% previous history of TB in their patients which is quite low than that of our study results. Different studies reported from all over the world have associated MDR TB with poor compliance with previous treatment of TB in the development of MDR<sup>11-19</sup>. Similar findings have been observed in our study where poor compliance with the treatment was more than 80%, good compliance with the treatment was present in only 28 (19.9%) of our study cases. Similar results have been reported by Rifat et al, Mulu et al and Li et al<sup>11, 17, 18</sup>. History of close contact with TB patient was reported by 92 (65.2%) of our study cases while Rifat et al<sup>17</sup> reported 39 % history of close contact with TB patients, 20 (14.2%) were defaulters and 42 (29.8%) presented with treatment failure. Mulu et al<sup>18</sup> reported 88 % defaulter rates in these patients. History of HIV infection was zero in our study, while different studies conducted in different parts of the world have found high frequencies of HIV infections among targeted population.

### CONCLUSION;

Previous history of Tuberculosis with poor compliance with drug therapy was the major risk factor for the development of MDR TB in our study. History of close contact with TB patients was another important risk factor in the development of MDR TB. Other important risk factors were previous history of tuberculosis infection, living in urban slum areas, poor educational status and poor socioeconomic status were more common.

### REFERENCES;

1. World Health Organization. WHO Report 2007. Global Tuberculosis Control. Surveillance, Planning, Financing. Switzerland:2007.
2. SAARC Tuberculosis Center. Tuberculosis in the SAARC Region-an update. Kathmandu, Nepal: SAARC Tuberculosis Center; 2009.
3. Goble M, Iseman MD, Madsen LA, Waite D, Horsburgh CR. Treatment of 171 patients with pulmonary tuberculosis resistant to isoniazid and rifampin. *New Engl J Med* 1993;328:5277-32.
4. World Health Organization. Anti-tuberculosis drug resistance in the world: fourth global report. Geneva:WHO,2008.
5. Caminero JA. Multidrug-resistant tuberculosis: epidemiology, risk factors and case finding. *Int J Tuberc Lung Dis*.2010;14(4):382-90.
6. Ejaz M, Rehana A, Sudduqui A, Rafiq Y, Malika F, Channa A. Prevalence of multi-drug resistant tuberculosis in Karachi, Pakistan: identification of at risk groups. *Trans R Soc Trop Med Hyg*.2010;104(8):511-17.
7. Javaid A, Hasan R, Zafar A, Ghafoor A, Pathan AJ, Rab A, et al. Prevalence of primary multidrug resistance to anti-tuberculosis drugs in Pakistan. *Int J Tuberc Lung Dis* 2008; 12:326-31.
8. Rajput MH, Memon KN. Frequency and Risk Factors for Multidrug Resistant Tuberculosis (MDR-TB) among patients Admitted at TB Sanatorium Kotri. *Pak J Chest Medicine* 2013;19(3): 104-09.
9. Pant R, Pandey KP, Joshi M, Sharma S, Pandey S. Risk Factor Assessment of Multidrug-Resistant Tuberculosis. *J of Nep Health Res Coun* 2009;7(2):89-92
10. Flora MS1, Amin MN, Karim MR, Afroz S, Islam S, Alama A, et al. Risk factors of multi-drug resistant tuberculosis in Bangladeshi population: a case control study. *BanglMed Res Coun Bull* 2013;39:34-41.
11. Li XX, Lu W, Zu RQ, Zhu LM, Yang HT, Chen C, et al. Comparing risk factors for primary multidrug-resistant tuberculosis and primary drug-susceptible tuberculosis in Jiangsu province, China: a matched-pairs case-control study. *Am J Trop Med Hyg*. 2015;92(2):280-5.
12. Marahatta SB. Multi-drug resistant tuberculosis burden and risk factors: an update. *Kathmandu Univ Med J (KUMJ)*. 2010;8(29):116-25.
13. Tanrikulu AC, Abakay A, Abakay O. Risk factors for multidrug-resistant tuberculosis in Diyarbakir, Turkey. *Med Sci Monit*. 2010;16:PH57-PH62.
14. Vadwai V, Shetty A, Soman R, Rodrigues C. Determination of risk factors for isoniazid mono-resistance and multidrug-resistant tuberculosis in treatment failure patients. *Scand J Infect Dis*. 2012;44:48-50.

15. Balaji V, Daley P, Anand AA, Sudarsanam T, Michael JS, Sahni RD, Chordia P, George IA, Thomas K, Ganesh A, John KR, Mathai D. Risk factors for MDR and XDR-TB in a tertiary referral hospital in India. PLoS ONE. 2010;5:e9527.
16. Liang L, Wu Q, Gao L, Hao Y, Liu C, Xie Y, et al. Factors contributing to the high prevalence of multidrug-resistant tuberculosis: a study from China. Thorax. 2012;67:632–638.
17. Rifat M, Milton AH, Hall J, Oldmeadow C, Islam MA, Husain A, et al. Development of multidrug resistant tuberculosis in Bangladesh: a case-control study on risk factors. PLoS One. 2014 Aug 19;9(8):e105214. doi: 10.1371/journal.pone.0105214.
18. Mulu W, Mekonnen D, Yimer M, Admassu A, Abera B. Risk factors for multidrug resistant tuberculosis patients in Amhara National Regional State. Afr Health Sci. 2015;15(2):368-77.
19. Wang K, Chen S, Wang X, Zhong J, Wang X, Huai P, et al. Factors contributing to the high prevalence of multidrug-resistant tuberculosis among previously treated patients: a case-control study from China. Microb Drug Resist. 2014;20(4):294-300.