WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH
www.wjpmr.com

FREQUENCY OF FACTORS LEADING TO MDR TB

Dr. Talha Bin Yousuf[1], Dr. Khair Un Nisa[2], Dr. Qaseem Ali Zaidi*[3]

[1]Nishtar Medical University and Hospital Multan.
[2]Multan Medical and Dental Collage.
[3]Rashid Latif Medical College Lahore.

*Corresponding Author: Dr. Qaseem Ali Zaidi

Rashid Latif Medical College Lahore.

ABSTRACT

Objective: The objective of this study is "to determine the frequency of factors leading to Multidrug resistance tuberculosis, in patients presenting at Nishtar Medical University and Hospital Multan". **Material and methods:** This cross sectional was conducting at Department of Pulmonology, Nishtar Medical University and Hospital Multan from March 2018 to September 2018. Total 126 patients with MDR-TB were selected for this study. Association of reasons for interruption of ATT course, inadequate chemotherapy, under whose prescription ATT used previously and Previous H/O of taking ATT with gender, age and area of residence was assessed. **Results:** Total 126 patients with MDR-TB were included in this study. Minimum age of the patients was 20 years and maximum age of the patients was 60 years. Mean age of the patients was 39.44 ± 9.043. Most 65 (51.6%) of the patients with MDR-TB belonged to age group 31-40 years and 74 (58.7%) were male and 52 (41.3%) were female. **Conclusion:** Results of this study revealed that the most common age group affected with MDR-TB was 31-40 years. Male were more victim as compare to female. Mostly patients reported with MDR-TB have previous history of taking ATT under.

KEYWORDS: MDR-TB. Multi-drug resistant tuberculosis. Factors, Primary MDR-TB, DOTS.

INTRODUCTION

Tuberculosis is a specific infectious disease caused by Mycobacterium Tuberculosis, primarily affect lungs. It can also affect intestine, meninges, bones and joints, lymph nodes and other tissues of body. The disease is usually chronic with varying clinical manifestations. Approximately one third of the world population having latent tubercle bacilli infection. Around 8 million new cases of active disease develop each year and 3 million people die.[1] In Pakistan its incidence is estimated to be 171/100,000 population.[2] Besides high incidence of tubercle bacilli in Pakistan, prevalence of multi drug resistant strains is also a cause of great concern.[3] Multi Drug Resistant Tuberculosis (MDR TB) is defined as "simultaneous resistance of mycobacterium tuberculosis to both isoniazid (NH) and rifampicin (RIF) with or without resistance to other anti-tuberculosis drugs.[4] "Patients infected with MDR strains are not only difficult to cure but also more likely to remain source of infection for a longer period of time than those with drug susceptible organisms.[5] At any given time about 630,000 people in the world are thought to carry strains of M. tuberculosis showing resistance to the two drugs that are currently the most effective against tuberculosis (TB): isoniazid and rifampicine.[6] So far, the magnitude of the problem posed by multidrug resistant TB (MDR

TB) has been estimated in about two thirds of all countries worldwide through disease surveillance and surveys. Each year, as more studies are conducted, new hot spots of MDR TB are documented.[7]

Tuberculosis continues to be a global public health problem. Drug resistance and obstacles to successful directly observed therapy short course (DOTS) impede disease control. Among patients being retreated for TB because of initial treatment failure, default from initial treatment or relapse following initial treatment, drug resistance is common and retreatment outcomes are inferior. Drug resistance is entirely a man-made problem and develops in otherwise treatable TB when the course of treatment is interrupted and the levels of drug in the body are insufficient to kill 100% of bacteria. This can happen due to number of reasons like inadequate chemotherapy, repeated intermittent courses of ATT, unsupervised treatment by general practitioner during initial course of ATT. Exposure to single drug due to irregular drug supply and poor compliance of patient suppresses the growth of bacilli susceptible to that drug but permits the multiplication of drug resistant organisms.[8]

Prevalence of some risk factors for multidrug resistant tuberculosis as in a study conducted at Tertiary Care

Hospital Peshawar are as previous history of taking ATT / repeated and intermittent courses of ATT(20% had undertaken ATT course once, 53.3% twice and 26.7% thrice in past), inadequate chemotherapy(43.3%), family history of tuberculosis(23.3%), and reasons for interruption of their treatment e.g. non affordability and having side effects(46.2% each) and feeling of no improvement(7.6%).[9]

Isoniazid is one of the most effective and specific agent for the treatment of the disease caused by Mycobacterium Tuberculosis. It is the corner stone of the modern short course chemotherapy for tuberculosis and also widely used to treat latent mycobacterium tuberculosis infection to prevent the active disease and the subsequent TB transmission.[10] Patients infected with a mycobacterium spp. Strain resistant to INH and RIF, which defines a MDR TB strain, do not respond to WHO standardized directly observed short course chemotherapy and require longer, more toxic and more expensive treatment. The only way to prevent TB entirely is to effectively treat the active cases, so as to stop the transmission of this infection in the community.[11, 12]

The increasing prevalence of infection with drug resistant Mycobacterium tuberculosis represents a global public health emergency as there is minimum work at local level. Determination of factors for MDR TB will help to stop the transmission of this infection in the community which will reduce the financial burden of community and as well as complication or side effects of the treatment would also be decreased.

Operational Definitions
Factor: Is any attribute, characteristic or exposure of an individual that increases the likelihood of developing a disease.

Inadequate Chemotherapy: Inadequate chemotherapy was labeled when there is administration of lower doses of ATT used or failure to complete the whole course of treatment.

Repeated or incomplete courses of ATT
Patient took treatment of TB once, twice or more and not complete the established course of treatment.

Non Affordability: It was labeled when there is interruption of ATT due to non-affordability. **Side effects:** It was labeled when there is interruption of ATT due to having side effects like vomiting (2 or 3 times a day) for at least one day

MATERIAL AND METHODS
This cross sectional was conducting at Department of Pulmonology, Nishtar Medical University and Hospital Multan from March 2018 to September 2018. Total 126 patients with MDRTB were selected for this study.

Inclusion criteria: All the patients of different age and sex from Pulmonology Department, Nishtar Medical University and Hospital Multan suffering from tuberculosis, whose AFB culture and sensitivity report revealed INH and RIF both resistance.

Exclusion criteria: All patients from Pulmonology Department, Nishtar Medical University and Hospital Multan suffering from tuberculosis whose AFB culture and sensitivity report revealed Mono drug resistant TB or Poly drug resistant TB but not Multi Drug Resistant TB. All those patients whose culture and sensitivity report was awaited or not available at time of interview was also be excluded.

Data Collection Procedure
Data was collected on a pre-designed pre-tested questionnaire. The data was regarding age, gender, family history of TB collected. History of tuberculosis in past, repeated or incomplete courses of ATT, inadequate chemotherapy, unaffordability and side effects were also be recorded. In patients having past history of TB, further information like under which supervision (DOTS, general physician, chest consultant, others) ATT was used, were also be recorded.

Data Analysis: The data were entered and analyzed in SPSS version 16. Mean and Standard Deviation was measured for quantitative data like age. Qualitative data were presented in percentages such as, gender, interruption due to side effects, non-affordability, inadequate chemotherapy and repeated and incomplete courses of ATT. Stratification with respect to age, gender and area of residence was done. Post stratification, chi square test was applied. P value less than and equal to 0.05 was taken as significant.

RESULTS
Total 126 patients with MDR-TB were included in this study. Minimum age of the patients was 20 years and maximum age of the patients was 60 years. Mean age of the patients was 39.44 ± 9.043. Patients were divided into different age group. Out of 126 MDR-TB patients 74 (58.7%) were male and 52 (41.3%) were female. Non-affordability was the reason in 60 (47.62) patients of which 37 (61.67%) were male and 23 (38.33%) were female. Side effects of ATT course was the reason for interruption of ATT course in 58 (38.1%) patients, of which 33 (56.9%) patients were male and 25 (43.1%) patients were female. Not improving was the reason of interruption of ATT course in 8 (6.35%) patients, 50% patients were male and 50% patients were female.

Statistically insignificant association of reasons for interruption of ATT course with gender was noted with p value 0.761. Statistically insignificant association of reasons for interruption of ATT course, inadequate chemotherapy, under whose prescription ATT used previously and Previous H/O of taking ATT with gender was noted. (Table 1).

Table No. 2 showing association of reasons for interruption of ATT course, inadequate chemotherapy, under whose prescription ATT used previously and Previous H/O of taking ATT with age groups. Table No. 3 showing association of reasons for interruption of ATT course, inadequate chemotherapy, under whose prescription ATT used previously and Previous H/O of taking ATT with area of residence.

Table 1: Association of reasons for interruption of ATT course, inadequate chemotherapy, under whose prescription ATT used previously and Previous H/O of taking ATT with gender.

Variables	Gender		Total	P. value
	Male (%)	Female (%)		
Reasons for interruption of ATT course				
Non-affordability	37 (61.67)	23 (38.33)	60 (47.62)	0.761
Side effects	33 (56.9)	25 (43.1)	58 (38.1)	
Not improving	4 (50)	4 (50)	8 (6.35)	
Total	74 (58.53)	52 (41.27)	126	
inadequate chemotherapy				0.519

Table 2: Association of reasons for interruption of ATT course, inadequate chemotherapy, under whose prescription ATT used previously and Previous H/O of taking ATT with age groups.

Variables	Age Group				Total	P. value
	20-30 (%)	31-40 (%)	41-50 (%)	51-60 (%)		
Reasons f or interruption of ATT course						
Non-affordability	5 (8.33)	28 (46.67)	16 (26.67)	11 (18.33)	60 (47.62)	0.338
Side effects	10 (17.24)	32 (55.17)	9 (15.52)	7 (12.07)	58 (46.04)	
Not improving	0	5 (62.5)	1 (12.5)	2 (25)	8 (6.35)	
Total	15 (11.9)	65 (51.59)	26 (20.63)	20 (15.87)	126	
in adequate chemotherapy						
Yes	8 (16)	24 (48)	12 (24)	6 (12)	50 (39.68)	0.455
No	7 (9.21)	41 (53.95)	14 (18.42)	14 (18.42)	76 (60.32)	
Total	15 (11.90)	65 (51.59)	26 (20.63)	20 (15.87)	126	
Under whose prescription ATT used previously						
DOTS	7 (12.73)	25 (45.45)	14 (25.45)	9 (16.36)	55 (43.65)	0.602
GP	6 (10)	35 (58.33)	9 (15)	10 (16.67)	60 (47.62)	
Chest Consultant	2 (20)	5 (50)	2 (20)	1 (10)	10 (7.94)	
Others	0	0	1 (100)	0	1 (0.79)	
Total	15 (11.90)	65 (51.59)	26 (20.63)	20 (15.87)	126	
Previous H/O of taking ATT						
Yes	14	58	21	14	107	0.133
No	1	7	5	6	19	
Total	15	65	26	20	126	
Yes	29 (58)		21 (42)	50(39.68)		
No	45 (59.21)		31 (40.79)	76(60.32)		
Total	74 (58.73)		52 (41.27)	126		
Under whose prescription ATT used previously						
DOTS	36 (65.45)		19 (34.55)	55 (4.37)		
GP	34 (56.67)		26 (43.33)	60(47.62)		0.261
Chest Consultant	4 (40)		6 (60)	10 (7.94)		
Others	0		1 (100)	1 (0.79)		

Total	74 (58.73)	52 (41.27)	126	
Previous H/O of taking ATT				0.564
Yes	63	44	107	
No	11	8	19	
Total	74	52	126	

Table 3: Association of reasons for interruption of ATT course, inadequate chemotherapy, under whose prescription ATT used previously and Previous H/O of taking ATT with area of residence.

Variables	Area of residence		Total	P. value
	Rural n (%)	Urban n (%)		
Reasons for interruption of ATT course				
Non-affordability	38 (63.33)	22 (36.67)	60 (47.62)	0.374
Side effects	35 (60.34)	23 (39.66)	58 (46.03)	
Not improving	3 (37.5)	5 (62.5)	8 (6.35)	
Total	76 (60.32)	50 (39.68)	126	
inadequate chemotherapy				
Yes	28 (56)	22 (44)	50 (39.68)	0.268
No	48 (63.16)	28 (36.84)	76 (60.32)	
Total	76 (60.32)	50 (39.68)	126	
Under whose prescription ATT used previously				
DOTS	33 (60)	22 (40)	55 (43.65)	0.168
GP	39 (65)	21 (35)	60 (47.62)	
Chest Consultant	3 (30)	7 (70)	10 (7.94)	
Others	1 (100)	0	1 (0.79)	
Total	76 (60.32)	50 (39.68)	126	
Previous H/O of taking g ATT				
Yes	65	42	107	0.815
No	11	8	19	
Total	76	50	126	

DISCUSSION

MDR-TB is an increasing global problem arising from a combination of physicians' error and patients' noncompliance during treatment of susceptible tuberculosis. Wild strains of Mycobacterium tuberculosis that have not been exposed to anti-tuberculosis drugs are almost never resistant.[8] In present study mean age of the patients with MDR-TB was 39.44 ± 9.043. Similar mean age (34.2 ± 15.3 years) of the patients with MDR-TB was reported by Wahab et al,[8] in their study conducted at Peshawar. Results of Present study revealed that out of 126 patients with MDR-TB, the most common (51.6%) age group was 31-40 years. In one study by Wahab et al,[1] the most common age group of patients with MDR-TB was 20-40 years which are similar with our study. Faustino et al,[13] reported that most of the patients with MDR-TB was below 65 years. In another study Moniruzzaman et al,[14] the most common (46%) age group of patients with MDRTB was 21-40 year. These findings are also in favor of my study.

In present study out of 126 patients with MDR-TB male are more common as compare to female 58.7% vs. 41.3%. Male patients with MDR-TB are prominent in our study. Faustino et al,[13] determined the risk factors for MDR-TB in six countries of Europe and found that MDR-TB patients were more likely to be male. Findings of this study are similar with present study. Moniruzzaman ET al,[14] also reported 55% male and 45% female patients with MDR-TB in their study. These findings are also comparable with my study. In another study, Mulu et al,[15] reported male predominance (57.5% vs. 42.5%) in patients with MDR-TB. These results are similar with my study.

In present study 69.8% patients were un-educated, 19% patients were under metric and 11.1% were above metric. Wahab et al,[8] reported in their study, 70% patients as un-educated, 26.7% under metric and 3.3% patients as above metric. Results of this study are in favor of our study. In another study by Moniruzzaman et al,[14] among the 295 patients with MDR-TB 58% patients were secondary or below secondary and 42% patients were above secondary.

In present study 59.5% patients were laborer, 7.9% were students, 10.3% were government employee, 3.2% were house wife and 19% patients belonged to different other occupations. In one study conducted at Peshawar by Wahab et al,[8] it was noted that 64.7% patients with MDRTB were laborer followed by 5.8% were students, 11.8% were Govt. employee and 17.7% patients were belonged to different other profession. These findings are comparable with my study. Mulu et al,[15] reported in his study that 8.5% patients with MDR-TB were students and 14.4% were employee and 19% were laborer. These results were also in favor of our study. In my study

60.3% patients belonged to rural area and 39.7% patients belonged to urban area. Similar results were reported by Mulu et al,[15] in their study. They found 25.5% patients belonged rural area and 75.5% patients belonged to urban area. Results of another study by Li W-B[16] were also in favor of my study. He noted 68.78% patients belonged to rural area and 39.22% patients belonged urban area. In study of Tadesse F et,[17] al 82.2% were urban residents whereas 17.8% came from rural areas. In my study total 84.9% patients were found with previous history of taking ATT. In one study by Tadesse F,[17] among the MDR-TB cases, 97% have previously been treated for TB. Results of this study are comparable with our study. But Baliza et al,[18] found 50% patients with previous history of ATT used which is in contrast with my study. Total 43.7% patients taking ATT under DOT previously, 47.6% patients used ATT prescribed by GP, only 7.9% patients taking ATT on prescription of chest consultant and 0.8% patient taking ATT by some other sources. Similar results were reported by Wahab et al,[8] they reported that 40% patients taking ATT under DOT, 46.7% by GP, 6.7% by Physician.

CONCLUSION

Results of this study revealed that the most common age group affected with MDR-TB was 31-40 years. Male were more victim as compare to female. Mostly patients reported with MDRTB have previous history of taking ATT under.

REFERENCES

1. Dye C, Williams BG.Criteria for the controle of drug resistant tuberculosis. Pros Nat'l Accad Sic USA, 2000; 97: 8180-5.
2. World Health Organization. Global tuberculosis controle; surveillance, planning, financing. WHO report, Geneva: World Health Organization, 2003.
3. Matter TO. Surveillance of tuberculosis transmission by chromosomal DNA fingerprinting. Infect DIs J P, 1997; 4: 3-5.
4. Mahmoud A. Multi- drug resistant tuberculosis. J Pak Med Assoc, 2001; 51: 204-5.
5. Green E, Nchbeleng, M, De Villiers, BR, Seen P, Lestoalo T, Hose A, Bessong P O, Ned R N. Drug susceptibility patterns of Mycobacterium tuberculosis in Mpumalanga Province, South Africa: Possible Guiding Dosing of Retreatment Regimen. J Health Pool Neuter, 2010; 28: 7–13.
6. *Global tuberculosis control* Geneva: World Health Organization, 2012. (WHO/HTM/TB/2012.6).
7. Signal M, van Geert W, Falcon D, Sismondi's C, Glazier P, Floyd K, et al. Surveillance of anti-tuberculosis drug resistance in the world: an updated analysis, 2007–2010. Bull World Health Organ, 2012; 90: 111–119. D.doi:10.2471/BLT.11.092585.
8. The WHO/IUATLD.Global project on anti–tuberculosis drug resistant surveillance: anti – tuberculosis resistance in the world. prevalence trends: report no.2: Geneva: World Health Organization, 2000; 20–5.
9. Frazil W, Sadie A, Naveen k. Risk factors for Multi-drug Resistant Tuberculosis in patients at Tertiary Care Hospital, Peshawar. JCPSP, 2009; 19(3): 162–164.
10. Hu, Y, Hogner, S, Jiang, Wei, Cu, B. Extensive transmission of isoniazid resistant Tuberculosis and its association with increased multidrug resistant TB in two rural counties of eastern China: a molecular epidemiological study. BML infectious diseases, 2010; 10: 43-49.
11. Hussain F. Drug resistant TB. Park Chest Med, 2001; 7 (Suppl): 17–8. Sandhu GK. Tuberculosis: Current Situation, Challenges and Overview of its Control Programs in India. J Glob Infect Dis., 2011; 3(2): 143–50.
12. Sandhu GK. Tuberculosis: Current Situation, Challenges and Overview of its Control Programs in India. J Glob Infect Dis., 2011; 3(2): 143–50.
13. Faustini A, Hall AJ, Percy CA. Risk factors for multidrug resistant tuberculosis in Europe: a systematic review. Thorax, 2006 Feb; 61(2): 158–63.
14. Moniruzzaman A, Elwood RK, Schuler M, FitzGerald JM. A population-based study of risk factors for drug-resistant TB in British Columbia. The International Journal of Tuberculosis and Lung Disease, 2006; 10(6): 631–8.
15. Mulu W, Kekkonen D, Yammer M, Admass A, Baer B. Risk factors for multidrug resistant tuberculosis patients in Amara National Regional State. African Health Sciences, 2015 May 28; 15(2): 368.
16. Li W-B, Zhang Y-Q, Xing J, Ma Z-Y, Qi Y-H, Li X-X. Factors associated with primary transmission of multidrug-resistant tuberculosis compared with healthy controls in Henan Province, China. Infectious Diseases of Poverty, 2015; 4(1): 14.
17. Tadesse F. Risk Factors for Multi-drug Resistant Tuberculosis in Addis Ababa, Ethiopia. Universal Journal of Public Health, 2015; 3(2): 65–70.
18. Baliza M, Bach AH, Quiroz GL de, Melon IC, Carencro MM, Albuquerque M de FPM, et al. High frequency of resistance to the drugs isoniazid and rifampicin among tuberculosis cases in the city of Cabot de Santo Agostinho, an urban area in northeastern Brazil. Revisit da Sociedade Brasilia de Medicine Tropical, 2008; 41(1): 11–6.