

Original Article

Treatment Strategies in Defaulters Among MDR TB Patients

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Background: Tuberculosis is a chronic disease and the most common cause of death while drug resistance in TB is a serious health issue throughout the world. Individuals with MDR TB treatment defaulters are focused with least priority due to number of administrative, low socioeconomic and resource issues.

Objective: To follow and locate, MDR TB treatment defaulters with an intention to bring them back on treatment.

Methods: This exploratory observational study was undertaken by Pakistan Health Research Council, TB Research Centre from July 2017 to April 2018 in collaboration with Department of Pulmonology, King Edward Medical University/Mayo Hospital, Lahore. Data was collected in the form of demographic characteristics like name, age, gender and those with previous history of treatment, contact, co-morbidities, smoking and socio economic status were noted. The data was entered and analysed by using IBM SPSS.

Results: A total of 41 patients were successfully followed of which 20 (48.8%) were males and 21 (51.2%) were females with male to female ratio of 1:1.05. Mean age of male patients was 35.85±12.60 years and female patients remained 39.8±15.04 years with an overall mean age of 37.87±13.88. A total of 11 (26.8%) patients were re-enrolled 3 (7.3%) had started their treatment from private clinics while same number of patients died after re-enrolment in hospital. High number of 15 (36.6%) patients did not re-enrolled as they were not willing to take further medicine.

Conclusion: Proper counselling and follow up of drug resistant MDR TB defaulters can bring them back to re-enrol for treatment. Most common reason of the patients to default from treatment was parenteral therapy.

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Introduction

Tuberculosis (TB) is a chronic disease and the most common cause of death because, it is one of the most serious infectious diseases with a substantial public health problem, due to its high risk of person-to-person transmission, morbidity and mortality in adults.¹ This disease affects the most vulnerable community like poorest and malnourished individuals. Global incidence rate of TB is still rising 1% every year due to rapid increase of disease in Africa. Pakistan ranks 6th amongst the six high TB burden countries which bear 60% load of new TB cases with a shocking death rate of 17% in children suffering from TB.² According to the World Health Organization Global TB report 2020, over all new TB cases were reported to be 562000 in a year and prevalence

of TB as 265/100000 is much higher as compared to Global prevalence of 130/1000003.

Drug resistance in TB is a serious problem throughout the world. World Health Organization (WHO) took an extraordinary step and declared TB to be global emergency long ago in 1993. Tuberculosis, a well-known bacterial disease for the last 5000 years, is still infecting nearly one third of world population with a daily addition of 5000 new cases and loss of two lives every third minute.⁴ Mycobacterium tuberculosis which shows resistant to both isoniazid and rifampicin with or without resistance to other drugs is called multi drug-resistant strains. Multi drug-resistant tuberculosis poses a major threat to treatment as resistant cases have a high mortality.³ However, a lot of strategies have been developed to diagnose and treat

the MDR TB patients as various MDR treatment centers have started their work in many tertiary care centers of country.

The incidence of multidrug resistant (MDR) TB is 4.2% among new TB cases, and 16% among re-treatment TB cases.³ According to available second line anti tuberculosis drug sensitivity reports, the prevalence of extensively drug resistant tuberculosis (XDR-TB) cases amongst the MDR-TB varies from 5%-15% around the world.⁵ Programmatic management of drug resistant TB (PMDT) sites is working at their best in various centers around Pakistan. Sufficient prompt diagnostic and treatment facilities for MDR TB patients are provided by cooperation of Global Fund in the country; even then mortality and loss to follow up are present. This default from treatment poses major challenge in control of MDR TB burden as an irregular treatment increase costs. Moreover, defaulter cases exist as a potential threat to transfer primary MDR TB. Such patients also experience elevated risk of recurrence and TB related mortality as they more often remain sick, endanger not only their own life but also continue spreading drug resistant strains via air born droplets.⁶

Despite all the work done individual treatment defaulters are focused with least priority due to number of administrative, economical and resource matters. Pakistan Health Research Council TB Research Centre is working in close association and providing diagnostic services to PMDT site Mayo Hospital. Aim of present study was to follow MDR TB treatment defaulters with an intention to bring them back on treatment.

Methods

This exploratory observational study was undertaken by Pakistan Health Research Council, TB Research Centre from July 2017 to April 2018 in collaboration with Department of Pulmonology, King Edward Medical University and PMDT site Mayo Hospital, Lahore. All the defaulted patients getting MDR TB treatment (Complete enumeration), from PMDT site, Department of Pulmonology; King Edward Medical University Lahore were included in this study.

Data was collected in the form of demographic characteristics like name, age, gender, address etc., Signs and symptoms like duration of cough, fever, expectoration, weight loss, anorexia etc., History like previous history of treatment, history of contact, history of other diseases, history of smoking and other addiction and socio economic status were noted.

A team consisting of MDR physician, Psychologist, Researcher (Principal investigator or co-principal investigator) and a treatment coordinator visited the

defaulters at their homes. Patients were interviewed and reasons for default were asked. Patients were guided about the importance of treatment and hazards of noncompliance. Case wise information was recorded in detail regarding the specific problems individually after socio-demographic tabulation and case series ascending pattern was followed. The data was entered and analysed by using IBM SPSS. Data for socio-demographic variables was described by using basic descriptive statistics as mean, median, standard deviations and frequencies as per nature of variable.

Results

A total of 327 patients were registered during January 2016 to January 2018 and total 48(14.6%) MDR TB patients who were lost to follow up was collected from PMDT site Mayo Hospital Lahore. On scrutiny and visiting it was explored that 3 patients were died, 2 patients were unreachable due to very long distance and 2 patients refused to see hence excluded. Remaining 41 patients were successfully followed of which 20 (48.8%) were males and 21 (51.2%) were females with male to female ratio of 1:1.05. Mean age of male patients was 35.85±12.60 years and female patients remained 39.8±15.04 years with an overall mean age of 37.87±13.88.

Table 1: Demographic Characteristics of Patients

Characteristics/ Variables	Gender						
	Male (N=20)		Female (N=21)		Total (N=41)		
	n	%	n	%	n	%	
District	Lahore	12	60.0	10	47.6	22	53.6
	Gujranwala	3	15.0	8	38.0	11	26.8
	Hafizabad	3	15.0	1	4.8	4	9.8
	Narowal	1	5.0	1	4.8	2	4.9
	Sheikhupur	1	5.0	1	4.8	2	4.9
Occupation	Govt Job	3	15.0	0	-	3	7.3
	House Wife	0	-	18	85.7	18	43.9
	Jeweller	1	5.0	0	-	1	2.4
	Labour	9	45.0	0	-	9	21.9
	S Guard	2	10.0	0	-	2	4.9
	Shop keeper	2	10.0	1	4.8	3	7.3
	Student	2	10.0	2	9.5	4	9.8
	Tailor	1	5.0	0	-	1	2.4
Education	≤ Primary	10	50.0	13	61.9	23	56.0
	Middle	5	25.0	6	-	11	26.8
	Matriculation	3	15.0	1	4.8	4	9.8
	Higher Above	2	10.0	1	4.8	2	4.9
Comor- bidities	Diabetes	1	5.0	5	23.8	6	14.6
	HCV	0	-	1	4.8	1	2.4
	HBV	0	-	0	-	0	-

Most of the patients (53.6%) belong to Lahore in present study. Almost all the patients fall in lower socioeconomic group with very less or no education was predominant feature. Six patients also have diabetes and one was Hepatitis C virus positive. Demographic data and co-morbidities are shown in Table I.

History, background of treatment categories, site of disease and drug resistance pattern of the patients were shown in Table II. Previous history of at least first line of ATT was present in 95.1% patients while 4.9% suffer from primary MDR TB. Around 24.3% patients in present study had also taken second line of ATT before registration at PMDT site. Most of 36.5% patients defaulted due to Injectable drugs in this study.

Mean of total approximate income of patients included in this study remained around rupees 9262 was very low and less than the minimum wage rate of rupees 14000/month for unskilled workers. On the other had mean number of households was as high as 6.93 per house.

Follow up outcome of the patients is shown in Table III. A total of 11 (26.8%) patients are re-enrolled and continue their treatment from PMDT site. Three (7.3%) have started their treatment from private

Table II: History and Background of Study Subjects

Variable/Question	Response	Frequency	Percentage
Previous History of anti TB treatment	Present	39	95.1
Previous History of second line anti TB treatment	Present	10	24.3
Categorization of Treatment Regimen	New	2	4.9
	Relapse	15	36.5
	Failure	8	19.5
	Defaulter	6	14.6
	Unknown	10	24.3
Site of Disease	Pulmonary	39	95.1
	Extra-pulmonary	2	4.9
Main Reason To Default	Injectable Drugs	15	36.5
	Long Treatment	4	9.8
	Long Traveling	5	12.2
	Side Effects	9	21.9
	Attitude of Staff	5	12.2
	Social Stigma	3	7.41

clinics and not willing to come to the hospital, while same number of patients died after re-enrolment in hospital. Five (12.2%) cases although re-enrolled but again defaulted after one month and 4(9.8%) patients

although brought to the hospital, re-assessed by MDR physician and had their GeneXpert test negative were not re-enrolled as all of them have taken treatment for more than 15 months. High number of 15 (36.6%) patients did not re-enrolled as they were not willing to take further medicine.

Each case of MDR TB defaulter has its own story some of which may be summarised here. In this regard a man who was graduate and doing a private

Table III: Follow up Outcome of study Subjects

Outcome	N	%
Re-enrolled	11	26.8
Re-enrolled in private clinics	3	7.3
Died after re-enrolment	3	7.3
Defaulted after re-enrolment during one month	5	12.2
Not re-enrolled due to GeneXpert Negative	4	9.8
Not re-enrolled their self	15	36.6

job, living in combine family system with his elder brothers as he lost his parents few years back. All the family personals were busy in their own jobs and no one left behind to care him except his sister or in laws. Their behaviour was also very much superficial as he was served meals like prisoners. No one visit him whole day as he was locked in a separate room on second floor of house which leads him to a severe depression and further psychosis. Family has no time to bring him in the hospital even after a month. Similarly, a 34 years' young man who has no previous history of ATT and developed primary MDR. He took regular treatment for several months and great family support in terms of behaviour was observed but whole family was very poor. He himself had to work a lot for their survival as social support was minimal. His children also had to work to support their father. In the meantime, his one-year-old daughter fell ill and he has no money to bring her in the hospital and borrowed a little amount for her treatment and worked for a month or so in return. But his daughter could not survive and his home was also drifted in flood. He and his family took protection in nearby village. He developed the depression but agreed to resume his treatment and successfully completed his treatment.

In this context a woman took treatment for about nine months when her femur of left leg was broken. She already had difficulties in transportation and reaching hospital. She did not agree to restart treatment however her GeneXpert test was negative for TB at the time of interview. A 22-year-old unmarried girl and her family had a terrible background. It was a middle class family and head of household was doing a job in post office. The family migrated from their village to

Lahore to acquire better education facilities. Unknowingly four sisters fell ill one after the other and all of them suffered from primary MDR TB. Previously they took private treatment for two girls and paid a heavy amount as the treatment was very much costly. Later third and fourth girls were registered at PMDT site of Mayo hospital. Unfortunately, one of the last two was died within two months after registration for treatment. This was a great dilemma for the family and thought developed in their back of mind was poor quality treatment. Although they do not have any scientific justification even then refused to take the treatment and whole family went back to their village. They were followed, interviewed and tried to be convinced but they agreed to take private treatment and doing well.

A 19-year-old married woman bearing a baby boy developed MDR TB and registered at PMDT site where biosafety measures were described which when imposed and her baby was kept separate from her. She did not bear this situation and reported the police that her baby has been snatched from her that lead to the separation and family was split. Similarly, a 24-year-old married woman likewise earlier case. Her parents were caring for her but in laws were not with great behavioural and financial issues. The family used to lie about their enrolment in other hospital which was not assured from site and brought back on treatment.

Hence

Discussion

Multiple factors are associated with patients defaulting from MDR TB treatment which includes, dissatisfaction from treatment, behaviour of health care workers, patient's own behaviour, mobility and travelling, low socio-economic status high doses of drugs and severe side effects^{7,8} as all of these prevail at some level in present study. Believe in traditional healers, visit to hakim or homeopaths are some other factors reported in other studies from same settings⁹ though are not found in this study. Previous history of treatment may be considered as an additional factor of default from treatment as 95% of the study subjects have previous history of at least taking first line of ATT and 24.3% had taken second line treatment also as the results are not comparable with the study on problems of MDR TB patients revealed far less previous history of ATT as only 52%.⁹

Variety of stories have been unleashed in present study, showing the misery and difficulties at individual level directly related to patient's own or its treatment supporter's behaviour. Problems of female patients are more related to their in laws as are reported previously whilst for males they vary case to case.

Feeling of being well due to relief from pain and symptoms provokes the patients to default from the treatment.¹⁰ Substance abuse has been revealed as an important factor for default from drug resistant TB treatment in a study⁷ is not in agreement with present study as only 2.4% defaulters were alcoholic and 4.9% were smokers.

Mean of total approximate income of households included in this study remained around rupees 15324 was very low with a wide range of 5000 to 50000, where more than one person participated in household earning however the minimum wage rate set by Government in budget 2017-18 is rupees 15000/month for unskilled workers.¹¹ Although many attractive incentives for each MDR TB patient and one treatment supporter are given at PMDT sites by National TB Control Program, Pakistan with the help of collaborative donors. These incentives include social support in terms of cash, fare charges, free treatment and diagnostic facilities including provision of one month drugs.¹² Two patients (4.8%) in present study showed primary drug resistant tuberculosis pose that the frequency of primary cases to adhere from treatment is low as compared to acquired drug resistant patients on the other hand primary drug resistant TB is also as low as 4.2% whilst acquired drug resistance is 16% are notable in this regard.³

Transmission of drug resistant TB has been observed in a family in this study is of great importance where two patients acquire primary MDR TB. A recent study from same settings has already reported transmission of simple TB in eight out of total thirteen households during a period of around two years.¹³ Role of infection control, patient's awareness about disease and its transmission and seriousness at all levels are necessary tools in controlling the transmission. Although implementation of infection control measures has been suggested by WHO in 2016 for prevention of TB at National and subnational levels but still "wait and see" phenomenon is dominant due to unforeseen reasons.¹³

Contact screening of MDR TB is quite an effective tool in active case detection and hence control the transmission. A study on active case detection of patients among household contacts screened 692 contacts of 112 index MDR TB patients and found 17 (2.4%) smear positive cases of which 4 (23%) were resistant to rifampicin by GeneXpert.¹⁴ Free service of home visits for collection of sputum specimen from symptomatic household contacts of registered drug resistant patients is provided by each PMDT site in this regard.¹² Still a high default rate of 14.6% in present study is a great dilemma and stimulates the need to expressive implementation of five principals

for prevention of TB proposed by National TB Control Program, Pakistan which include early detection, infection control, strengthening of health system, underlying risk factors and social determinants especially last two are more studied in presently.

Conclusion

Proper counselling and follow up of drug resistant TB defaulters can bring them back to re-enrol for treatment either at PMDT site or privately as per convenience and resources of patients. Most of the patients in present study defaulted due to parenteral therapy followed by length of treatment and long traveling distance to secure drugs. National TB Control program has already started short term regimen (STR) for MDR TB patients by inducting two new drugs Bedaquilline and Delamanid at PMDT sites which is expected to improve the patients compliance.

Conflict of Interest: None

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References

1. Zaman K. Tuberculosis: A global health problem. *J Health Popul Nutr.* 2010; 28(2): 111–13.
2. World Health Organization. Tuberculosis fact sheet. [Updated 2019, Cited 2021] Available from: [<http://www.who.int/mediacentre/factsheets/fs104/en/>]
3. Global tuberculosis report 2020. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO.
4. National TB Control Program. Available from website updated January 2014: [www.ntp.gov.pk]
5. Migliori GB, Loddenkemper R, Blasi F, Ravigion M C. 125 years after Robert Koch's discovery of the tubercle bacilli: the new XDR threat. Is "science" enough to tackle the epidemic? *Eur Rep J* 2007; 294:23-7.
6. Shringarpure KS, Isaakidis P, Sagili KD, Baxi RK. Loss to follow up in multidrug resistant tuberculosis Treatment in Gujarat, India: The WHEN and WHO of It. *PLOS ONE.* 2015;10(7):doi:10.1371/journal.pone.0132543
7. Sanchez-Padilla E, Marquer C, Kalon S, Qayyum S, Hayrapetyan A, Varaine F, Bastard M, Bonnet M. Reasons for defaulting from drug-resistant tuberculosis treatment in Armenia: a quantitative and qualitative study. *Int J Tuberc Lung Dis.* 2014;18(2):160-7.
8. Holtz TH, Lancaster J, Laserson KF, Wells CD, Thorpe L, Weyer K. Risk factors associated with default from multidrug-resistant tuberculosis treatment, South Africa, 1999–2001. *Int J Tuberc Lung Dis.* 2006 ;10(6):649-55.
9. Rehman S, Munir MK, Iqbal R, Saeed S. Problems faced while treating multidrug resistant TB patients in a tertiary care setting. *J Int Academic Res Multidisciplinary.* 2018; 6(1): 65-74.
10. Munir MK, Iqbal R, Shabbir I, Chaudhry K. Factors responsible for failure to initiate tuberculosis treatment among smear positive tuberculosis patients. *Pak J Med Res.* 2012;51(2):34-7.
11. Minimum Wages in Pakistan with effect from 01-07-2017 to 30-06-2018. [updated November 2017, Cited April 2018. Available from website:[<https://paycheck.pk/main/salary/minimum-wages>]
12. Munir MK, Rehman S, Iqbal R. Meeting the challenge, making a difference: Multidrug resistance tuberculosis in Pakistan. *Pak J Med Res.* 2018; 57(1): 1-2.
13. Muhammad KM, Sana R, Rizwan I. A Need for Tuberculosis Infection Control Measures: A Case Series Study in Pakistan. *Asian Journal of Medicine and Biomedicine.* 2017;1(1):19-22.
14. Rehman S, Munir MK, Iqbal R, Salam AA, Saeed S, Masud F, Aasim M. Active case detection among household contacts of multi drug resistant tuberculosis patients in a tertiary care setting. *Pak J Med Res.* 2014;53(3):55-9.