JOURNAL OF INTERNATIONAL ACADEMIC RESEARCH FOR MULTIDISCIPLINARY
Impact Factor 4.483, ISSN: 2320-5083, Volume 6, Issue 1, February 2018

PROBLEMS FACED WHILE TREATING MULTIDRUG RESISTANT TB PATIENTS IN A TERTIARY CARE SETTING

SANA REHMAN*
MUHAMMAD KASHIFMUNIR**
DR. RIZWANIQBAL***
MUHAMMAD AASIM****

*Research Officer, PHRC TB Research Centre, King Edward Medical University, Lahore, Pakistan
**Research Officer, PHRC TB Research Centre, King Edward Medical University, Lahore, Pakistan
***Research Director, PHRC TB Research Centre, King Edward Medical University, Lahore, Pakistan
****Statistical Officer, PHRC TB Research Centre, King Edward Medical University, Lahore, Pakistan

Abstract

Tuberculosis is one of the main leading causes of death globally, with approximately two billion people get infected and two million annual deaths attributable to it. Multidrug resistant tuberculosis is worldwide and reasons behind this type of TB are inadequate or partial treatment, inappropriate regimen, non-standardized dosage and duration of medication. To study the Problems faced while treating Multidrug resistant TB Patients in a Tertiary Care Setting: A pilot study. This Descriptive study was carried out at PHRC TB Research Centre in collaboration with Institute of pulmonology, King Edward Medical University/Mayo Hospital, Lahore. A semi structured questionnaire was used to collect the information regarding demographic characteristics and presenting complaints. Data was entered and analyzed using SPSS V. 20. A total of 50 patients seeking treatment from PMDT site Mayo hospital Lahore were interviewed with male to female ratio of 1:1.38 in present study. An overall mean age of patients was 25.9±10.4 years. On average 44.9±42.8km distance traveled by each patient, mostly 60% patients use public transport. Mean expense of each patient to reach PMDT site remained 807.8±1096.5 with median of 350 and range of 60 to 6000 rupees. Similarly patients and attendants visit from far areas also spend mean amount of 394±167 with range of 100-600 rupees on meal. Attitude of health care workers at treatment site was reported very good by 42% patients while poor by 6% patients. Misbehave from household members was also observed in 16% of patients. High cost and inconvenience is being faced by the patients due to long traveling distance and scarce number of PMDT sites. Insufficient financial supports for food, travel cost, side effects of ATT, misbehave from spouse, family members and health care workers may be the reasons for noncompliance.

Keywords: Tuberculosis, Problems, Multidrug resistant, ZN Stain.

1. Introduction

Tuberculosis (TB) is a leading cause of illness and death worldwide. Approximately two billion people are infected worldwide and approximately two million annual deaths is attributed to it. In 2010, approximately 1.4 million people (range, 1.2-1.5 million) died of TB while in 2011; 5.8 million newly diagnosed cases were notified to National TB control programs (NTPs) and reported to WHO(1). The incidence of Multi-Drug Resistant (MDR) TB is 2.8% among new TB cases, and 35% among re-treatment TB cases(2).In 2013, the World Health Organization (WHO) reported that there were 3.7% MDR TB among new cases and about 20% in previously treated cases. WHO also estimated that there are 0.5 million new MDR-TB cases and 60% of which occur in Brazil, India, China, Russian Federation and South Africa till 2011(3). Directly observed short course treatment (DOTS) recommended by World Health Organization (WHO) has been expanded throughout the health services of the country since 2005, However the emerging problem of multi drug resistant (MDR) TB is attributing to compromise the TB controls programs(4).

MDR-TB is defined as those mycobacterium tuberculosis strain which are resistant to isoniazid and rifampicin simultaneously with or without resistant to other anti-tuberculosis agents. MDR TB is worldwide and reasons behind this type of TB are inadequate or partial treatment, inappropriate regimen, non-standardized dosage and duration of medication[4]. Hence the presence of such cases in the community can ultimately spread the resistant strains of TB to the healthy individuals. There is an urgent need for dramatic scale-up of access to effective MDR-TB and XDR-TB management(5). The highest proportion of MDR-TB cases has been reported from India, China, the Russian Federation, South Africa and Bangladesh(6). MDR-TB poses a significant global and public health concern, because of low efficacy rates for first line treatment regimens, 18 to 24 months of treatment and association with considerable mortality worldwide(7,8). An additional concern is the persistence of high or increasing incidence and spread of MDR-TB in industrialized and the developing world, related to poverty, migration, ethnic conflicts, substance abuse and the increase in HIV infection, sometimes coupled with the poor performance of national programs. These factors may lead to the development or increase of MDR which, however, is susceptible to proper health control measures(9).

Various factors attribute a negative impact on treatment success. These factors include social, personal, medicinal, comorbidities or other domestic issues which have been either neglected or difficult to address. It is therefore important to find out such kind of issues and

needed to address as early as possible for the sake of humanity from deadly MDR TB. A study on knowledge of about TB in Pakistan and concluded that population has misconception and poor knowledge about the disease(10).

Early management of MDR TB is a big challenge as Pakistan stands fourth in high burden of MDR TB. In such conditions it is necessary to know about the difficulties as well as problems faced by MDR TB patients. Rate of Co-infections and various challenges could be brought on surface regarding such patients. Aim of this study was to study the Problems faced while treating Multidrug resistant TB Patients in a Tertiary Care Setting: A pilot study

2. Methodology

This descriptive study was carried out at PHRC TB Research Centre in collaboration with Institute of Chest Medicine, King Edward Medical University/Mayo Hospital, Lahore. This study is completed within one year. Confirmed MDR TB patients who are already seeking their treatment form inpatients and outpatients of TB ward in Mayo Hospital, Lahore and started their treatment during year 2013 were included in present study.

A total of 50 confirmed MDR TB patients who started their treatment during year 2013 were enrolled in present study. Convenient sampling technique was used to collect data. Confirmed MDR TB patients and seeking the treatment from at least one year were included in present study.

A pre designed questionnaire was used to collect the information regarding demographic characteristics, socio economic status, previous treatment history before starting MDR treatment, presenting complaints, history of other chronic illnesses like hypertension, diabetes, hepatitis B &C, Renal disorders, eye sight complications, ear complications, gastric and skin problems. Other difficulties like social stigma, intervention of non-qualified practitioners, intervention of other home mates, and believes in religious healers etc. was recorded. ZN smear results of each month, treatment compliance and drug sensitivity testing for second line drugs was also noted. Other lab findings (Like LFT's, RFT,s and Ultrasound etc.) for vital organs suggested by MDR physician which are being performed during treatment were also noted. Data was entered and analyzed using SPSS V. 20.

3. Results

A total of 50 patients seeking treatment from PMDT site Mayo hospital Lahore were interviewed including 21(42%) males 29(58%) females with male to female ratio of 1:1.38 in present study. An overall mean age of patients was 25.9±10.4 years. Mean age of females

was 23.2±7.6 is lower compared to male patients which were 29.5±12.7. Various age groups, marital status, education and district of residence of study subjects are shown in table I.

Table I: Demographic Characteristics of MDR TB Patients (N = 50)

Characteristics		Gender					
		Male (N= 21)		Female (N= 29)		Total (N= 50)	
		N	%	N	%	N	%
Age Range (in years)	<= 20	7	33.3	15	51.7	22	44.0
	21 - 30	7	33.3	10	34.5	17	34.0
	31 - 40	3	14.3	2	6.9	5	10.0
	41 - 50	2	9.5	2	6.9	4	8.0
	51+	2	9.5	0	0.0	2	4.0
Marital Status	Married	12	57.1	19	65.5	31	62.0
	Unmarried	9	42.9	10	34.5	19	38.0
Education	Illiterate	11	52.3	15	51.7	26	52.0
	Primary	5	23.8	5	17.2	10	20.0
	Middle	2	9.5	4	13.7	6	12.0
	Higher Above	3	14.3	5	17.2	8	16.0
District of Residence	Gujranwala	4	19.0	9	31.0	13	26.0
	Lahore	14	66.7	14	48.3	28	56.0
	Others	3	14.3	6	20.7	9	18.0
History of Present Illness		8	38.1%	11	37.9	19	38.0
History of ATT		11	52.4%	15	51.7	26	52.0

Table II shows socioeconomic status of patients. Most of the patients (32%) were house wives and similar frequency of patients was jobless (32%). High number of 26(52%) patients were living in semi-furnished homes while only 4% patients were living in furnished and rest of 44% were living in non-furnished homes. Thirty six (72%) of the patients had no vehicle to travel thus use public transport. Twenty eight (56%) patients had their family income of rupees less than 15,000 and 96% of them had no other financial resources like cattle, farming etc. Regarding home appliances, patients responded that 54% had electric water pumps, 32% had washing machine, 8% had room cooler while only 2% had all these facilities at their home. Mean family size of patient was 7.2±3.0 with range of 1-18 households.

Table II: Socio-Economic Status of Study Subjects

Characteristics		Gender					
		Male (N= 21)		Female (N= 29)		Total (N= 50)	
		N	%	N	%	N	%
Job Nature	Business	1	4.8	0	0.0	1	2.0
	Govt. Employee	0	0.0	1	3.4	1	2.0
	Private Employee	5	23.8	1	3.4	6	12.0
	Daily wages	9	42.9	1	3.4	10	20.0
	House Wife	0	0.0	16	55.2	16	32.0
	Jobless	6	28.6	10	34.5	16	32.0
Residence	Furnished	1	4.8	1	3.4	2	4.0
	Semi-Furnished	8	38.1	18	62.1	26	52.0
	Non-Furnished	12	57.1	10	34.5	22	44.0
Nature of Vehicle	Car	0	0.0	1	3.4	1	2.0
	Bike	3	14.3	5	17.2	8	16.0
	Bicycle	2	9.5	3	10.3	5	10.0
	None	16	76.2	20	69.0	36	72.0
Approximate Income of Household	<7000	8	38.1	5	17.2	13	26.0
	7001-15000	7	33.3	18	62.1	25	50.0
	15001-25000	5	23.8	4	13.8	9	18.0
	25001-40000	1	4.8	2	6.9	3	6.0
	>40000	0	0.0	0	0.0	0	0.0
Other Financial Resources	Cattle	2	9.5	0	0.0	2	4.0
	Forming	0	0.0	0	0.0	0	0.0
	Small Industry	0	0.0	0	0.0	0	0.0
	Other	19	90.5	29	100.0	48	96.0
Family Size	<= 4	5	23.8	3	10.3	8	16.0
	5 - 8	11	52.4	22	75.9	33	66.0
	9 - 12	3	14.3	3	10.3	6	12.0
	13 +	2	9.5	1	3.4	3	6.0

History of other chronic illnesses was also recorded. Ten (20%) of the patients had hypertension, three (6%) were suffering from diabetes, two had hepatitis-B and one each was patient of hepatitis-C and chronic renal disease.

Eight (16%) patients also believe in religious healers/spiritual leaders and also visited them for treatment of TB while 11 (22%) of the patients visited to traditional healers that include formal medical practitioner (2%), Hakim (14%) and homeopathic (4%). Misbehave from household members was also observed in 8(16%) of patients out of which 7 patients were married females. All these patients were ignored by their spouse and behaved by their in

laws brutally. Due to this social stigma 6 of them were living with their parents. Even worse was that 2 patients were divorced and 2 were separated from their parents due to their illness. One male patient was also separated from his family due to MDR TB. There were 11 (22%) students who had to stop their education and 2 patients lost their job due to MDR TB in this study.

Table III shows transportation and economic problems of patients while taking MDR TB treatment. On average 44.9±42.8km distance traveled by each patient to reach the PMDT site for taking drugs with a wide range of 3-200km. Most of 98% of patients received their medicine in single visit on same day. Mostly 60% patients use public transport to reach PMDT site followed by26% private and 14% use their personal transport. About 42% patients had to bring their attendant necessarily due to various social issues which ultimately affects the daily wages of attendant. Mean expense of each patient to reach PMDT site remained 807.8±1096.5 with median of 350 and range of 60 to 6000 rupees. Similarly patients and attendants visit from far areas also spend mean amount of 394±167 with range of 100-600 rupees on meal.

Table III: Transportation and Economic Problems of MDR TB patients. (N=50)

Characteristics		Gender					
		Male (N= 21)		Female (N= 29)		Total (N= 50)	
		N	%	N	%	N	%
Frequency of Monthly Visits	once	21	100.0	28	96.6	49	98.0
	Twice	0	0.0	0	0.0	0	0.0
	More	0	0.0	1	3.4	1	2.0
Type of Vehicle Used	Personal	4	19.0	3	10.3	7	14.0
	Public	13	61.9	17	58.6	30	60.0
	Private	4	19.0	9	31.0	13	26.0
Need Attendant		5	23.8	16	55.2	21	42.0
Attendant Working		3	14.3	6	20.7	9	18.0
Got Admitted in Hospital		4	19.0	2	6.9	6	12.0
Received Medicine From PMDT Site		21	100.0	29	100.0	50	100.0

Table 4 shows social issues regarding PMDT site healthcare workers with patients. Attitude of health care workers at PMDT site was reported very good by 42% patients. Only 6% patients reported poor attitude of healthcare staff however not specified the person. All patients acquire the medicine from PMDT site without any hurdle though one (2%) patient had to visit twice to receive medicine.

Table IV: Attitude of Health Care Workers.

Characteristics		Gender					
		Male (N= 21)		Female (N= 29)		Total (N= 50)	
		N	%	N	%	N	%
Attitude of Health Care Staff	Very Good	10	47.6	11	37.9	21	42.0
	Good	6	28.6	9	31.1	15	30.0
	Average	4	19.1	3	10.4	7	14.0
	Poor	1	4.8	2	6.9	3	6.0

Table V shows adverse reactions due to ATT. Hearing problem was observed in 17 (34%) patients while no complete haring loss was observed. Similarly 5 (10%) patients had vision problem, nausea 29 (58%) irritation 13 (26%) and 15 (30%) patients showed weakness and lethargy. Another adverse reaction observed due to ATT was joint pain 26 (52%) however none of the patient feel trembling of hand during their treatment .Only 2 (4%) patients had swelling on face and ankle. Unusual bleeding /bruising were not observed in any patient while only 1 (2%) patient suffers from bloody urine.

Table V: Adverse Reaction Due to ATT.

Characteristics	Gender					
	Male (N= 21)		Female (N= 29)		Total (N= 50)	
	N	%	N	%	N	%
Hearing Problem	8	38.0	9	31.1	17	34.0
Vision Problem	2	9.5	3	10.3	5	10.0
Feel Nausea	10	47.6	19	65.5	29	58.0
Fell Irritation	3	14.3	10	34.5	13	26.0
Feel Weakness/Lethargy	6	28.6	9	31.0	15	30.0
Joint Pain	11	52.4	15	51.7	26	52.0
Have Swelling on Face or Ankle	2	9.5	0	0.0	2	4.0
Suffer From Bloody/Cloudy Urine	0	0.0	1	3.4	1	2.0

Few patients who are receiving ATT complain of hearing problem, accordingly their doses of different drugs are adjusted or deleted as below after performing audiometry. If mild hearing loss was observed the dose of Amikacin is reduced, if moderate, sever or profound hearing loss observed then amikacin is replaced with capreomycin. If vision problem is observed patient is referred to ophthalmology for further diagnosis of cataract, if no cataract is reported then ethionamide is stopped. In case of nausea, vomiting, timing of ethionamide is shifted to night time and gravinate is added. Symptomatic treatment is advised in case of all other side effects and doses of different drugs are adjusted.

4. Discussion:

Mean expense of patients to reach PMDT site was 807.8± 1096.5 with median of 350 and range of 60-6000 rupees in present study. Although NTP has started to support the patients through global fund resources (11) however 600 rupees per month are provided for each patient to reach treatment facility are less than the average expenses presented in current study. Similarly average expense on meal remained 394±167 with range of 100-600 rupees for one patient and attendant while food financial support provided in terms of food basket against one registered MDR TB case is 4494 rupees making 74 rupees per person per day is not sufficient either(12). Transportation subsidy initiative to support poor TB patients has been started in poor areas of China TB control program since 2007. Evaluation of this project revealed that the subsidy had an important part in minimizing financial problems of poor patients for success of treatment and proposed a universal and balanced amount for transportation should be provided (13).

Average distance travelled by each patient to reach PMDT site for taking treatment remained 44.9± 42.8 with range of 3-200 km shows that a PMDT site covers wide area to facilitate MDR TB patients. As the study results shows that 72% patients had no personal vehicle thus use public transport to reach PMDT site. This situation may not only increase the suffering of MDR TB patient but increase the potential threat for general public also. There are no clear policies for MDR TB patients regarding use of public transport as they are infectious (14). It has been suggested that to educate the patient to avoid public places until sputum smear becomes negative is compulsory(14). Concerning the educational level and socioeconomic status of patients in current study, it is not easy for the patients arrange private transportation.

Misbehave from house hold members were also observed in 16% of patients in present study. Sufferers include 14% married females and 12% were living with their parents instead of spouse. Results of present study are not comparable with a study from New Delhi which revealed 94.6% of households and 92% of male spouse remained supportive with patients moreover male spouse remained more supportive (94.5%) as compared to female spouse (88.6%) (15). Believe in religious leaders and traditional healers for treatment of TB is another important problem, as in present study 22% patients visited traditional healers including hakims and homeopathic treatment while 16% visited to spiritual leaders for treatment of MDR TB. Results of this study are not in agreement with previous study from same settings on defaulters TB patients that presented 82% patients believing upon such healers (16).

Poor and average attitude from healthcare staff was reported by only 6% and 14% MDR TB patients respectively, results are comparable with an older study (16). Hearing problem has been reported due to use of kanamycin, amikacin and streptomycin. A comprehensive review reported an ototoxicity range of 2.6-46.5% among patients treated for MDR TB (17) was in accordance with present study that reported hearing problem of 34% among respondents. Nausea was reported in 58% remained highest side effect followed by Joint pain 52%, weakness and lethargy in 30%, irritation among 26% patients in present study. Second line anti-tuberculosis drugs that cause nausea include ofloxacin, levofloxacin, cycloserine, aminoglycosides and capreomycin. Main causative agents of joint pain and skin problems include pyrazinamide, Ethambutol and isoniazid (18).

5. Conclusion:

High cost and inconvenience is being faced by the patients due to long traveling distance due to the scarce number of PMDT sites. Insufficient financial support for food and travel cost may be the reasons for non-compliance. Sometime misbehaving attitude of health care workers with patients, unreasonable behavior of spouse and family members is disturbing. Misbelieves about treatment and side effects of ATT may be the reasons of poor compliance.

5.1. Recommendations/suggestions

1. Number of PMDT sites must be increased to minimize the traveling distance of patients and transportation charges of patients must be adjusted to acceptable level of private vehicle which ultimately control the spread of drug resistant bacilli.
2. Misbehave from spouse and in laws, believe in religious, spiritual and non-medical practitioners must be controlled by proper counseling of patients as well as attendants with psychologist.
3. Management of adverse reactions due to medicines must also be controlled by proper counselling with patients and provided guidelines to control them.

Acknowledgements

We acknowledge Pakistan Health Research Council for the funding of this project.

References:

1. Asif M. Incharge PMDT site Mayo Hospital, Lahore. Personal communication May 10, 2017.
2. Dhingra, V. K., & Khan, S. (2010). A sociological study on stigma among TB patients in Delhi. Indian J Tuberc. 2010; 57:12-18.
3. Drobniewski, F., Balabanova, Y., Nikolayevsky, V., Ruddy, M., Kuznetzov, S., Zakharova, S., ...&Fedorin, I. (2005). Drug-resistant tuberculosis, clinical virulence, and the dominance of the Beijing strain family in Russia. *Jama*, *293*(22), 2726-2731..
4. Gilani, S. I., &Khurram, M. (2009). Perception of tuberculosis in Pakistan: findings of a nation-wide survey. *Age (Years)*, *30*(965), 35.
5. Global Tuberculosis Control: WHO Report 2011. (2011) Available1. from: http://www.who.int/tb/publications/global_report/2011/gtbr11_main.pdf, accessed on December 22, 2012.
6. Guidelines for the Management of Adverse Drug Effects of Antimycobacterial Agents. [Updated 1998, cited 2017] Available from website: [http://www.uphs.upenn.edu/TBPA/treatment/managingsideeffects.pdf]
7. Gupta, R., Kim, J. Y., Espinal, M. A., Caudron, J. M., Pecoul, B., Farmer, P. E., &Raviglione, M. C. (2001). Responding to market failures in tuberculosis control. Science.293(5532):1049-51.
8. Mlambo, C. K., Warren, R. M., Poswa, X., Victor, T. C., Duse, A. G., & Marais, E. (2008). Genotypic diversity of extensively drug-resistant tuberculosis (XDR-TB) in South Africa. *The international journal of tuberculosis and lung disease*, *12*(1), 99-104.
9. Multi drug resistant tuberculosis available at [http://www.doh.gov.za/docs/policy/2011/policy_TB.pdf]
10. Multi-Drug Resistant tuberculosis (MDR-TB) Update. Available from: http://www.who.int/tb/challenges/mdr/MDR_TB_FactSheet.pdf
11. Munir, M. K., Iqbal, R., Shabbir, I., &Chaudhry, K. (2012). Factors responsible for failure to initiate tuberculosis treatment among smear positive tuberculosis patients. *Pakistan Journal of Medical Research*, *51*(2), 34-37.
12. National TB Control Program. Facts DR-TB. [updated 2015, Accessed May 2017] Available from: [http://www.ntp.gov.pk/departmentDetail.php?did=18&page=52]
13. Seddon, J. A., Godfrey-Faussett, P., Jacobs, K., Ebrahim, A., Hesseling, A. C., &Schaaf, H. S. (2012). Hearing loss in patients on treatment for drug-resistant tuberculosis. *European Respiratory Journal*, *40*(5), 1277-1286.
14. Shin, S. S., Furin, J. J., Alcántara, F., Bayona, J., Sánchez, E., &Mitnick, C. D. (2006). Long-term follow-up for multidrug-resistant tuberculosis. *Emerging infectious diseases*, *12*(4), 687.
15. White L. TB control in the public transport industry. [Updated on June 2015, accessed May 2017] available from website: [https://www.ghdonline.org/ic/discussion/tb-control-in-the-public-transport-industry/]
16. World Health Organization global tuberculosis report 2012 Available from [http://www.who.int/tb/publications/global_report/gtbr12_main.pdf]
17. World Health Organization. Global tuberculosis control: epidemiology, strategy, financing. WHO report 2009 (WHO/HTM/TB/2009.411). Geneva: World Health Organization; 2009.
18. Zhao, Q., Wang, L., Tao, T., &Xu, B. (2013). Impacts of the “transport subsidy initiative on poor TB patients” in Rural China: A Patient-Cohort Based Longitudinal Study in Rural China. *PLoS One*, *8*(11), e82503.