Original Research Paper

A Study to Identify the Factors Responsible for the Delay in Treatment Initiation of MDR-TB Cases Registered Under RNTCP in a District of South India

Medical Science

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ABSTRACT
Background: The economic burden to manage Multi-drug resistant Tuberculosis (MDR-TB) cases is very high as the average cost of drugs alone for treating MDR-TB patient is 50 to 200 times higher than for treating a drug-susceptible TB patient. If left undiagnosed or poorly treated, MDR-TB patients often live and suffer for years before succumbing to the disease and hence transmission of multi-drug resistance strains can continue, amplifying the multi-drug resistance in the community. Timely identification of MDR-TB cases and prompt initiation of treatment is crucial to prevent the transmission of disease and reduce the associated high morbidity and mortality. Hence, this study was conducted to find out the factors for the delay in treatment initiation of MDR-TB Cases. *Methodology:* The present study was a Community based Cross-sectional study conducted among the MDR-TB Patients registered under RNTCP in all the 9 Tuberculosis Units (TUs) of Krishna District, Andhra Pradesh from November 2012 to October 2014. The total number of study participants that were interviewed were 97 after applying inclusion and exclusion criteria .The perceptions of the MDR-TB patients and the Key staff of District TB Office, Krishna District have also been obtained regarding treatment delay. *Results:* Males were 68% of the total subjects and most (68%) of them belong to "rural" background. Most (85%) of the study subjects belong to the lower Socio-Economic Status (SES) and a majority (81%) belong to the "Hindu Religion". About 35% of MDR-TB patients belong to "Unskilled" occupation group while 31% belong to "Unemployed" occupation group. Majority of the study subjects were "married" (88%) and the educational status was below primary level in 71% of them. *Conclusion:* The factors that were found statistically significant for treatment delay were presence of co-morbid illness, alcohol consumption, lack of family support, long distance of Drug Resistant TB centre (DR-TB) centre from patient's residence and Lower Socio-Economic Status (SES)

Introduction

According to the WHO, globally, there are an estimated 8.6 million people who developed TB and 1.3 million died from this disease in 2012, of which, India alone accounts for 26% of the total cases. Annually, there are an estimated new cases of about 450000 of MDR-TB that occur worldwide every year and an estimated 170000 deaths from MDR-TB[1]. In India, the estimated prevalence of MDR-TB is found to be 1 to 3% in new cases and around 12% in previously treated cases as per the Drug Resistance Surveillance (DRS) studies conducted by RNTCP countrywide[2]. Undiagnosed, untreated or improperly treated patients with MDR-TB are a source of ongoing transmission of resistant strains within the community, resulting in future added costs and mortality. If left undiagnosed or poorly treated, MDR-TB patients often live and suffer for months to years before succumbing to the disease and hence transmission of multi-drug resistance strains can continue, amplifying the multi-drug resistance in the community. Hence, timely identification of MDR-TB cases and prompt initiation of treatment is crucial to prevent the transmission of disease and reduce the associated high morbidity and mortality[3]. As a very few studies have been conducted to find out the delay in initiation of treatment of MDR-TB cases in India, and none of the study of this kind was done in Krishna District, Andhra Pradesh (AP), this study was done to identify the various factors responsible for the delay in initiation of treatment of MDR-TB cases in Krishna District, AP.

Objectives of the Study:

1. To identify the factors (both the patient and health system related factors) leading to the delay in treatment initiation of MDR-TB cases.
2. To determine the socio-demographic factors among the study participants.

Methodology

The present study was a Community Based Cross Sectional Study conducted for a period of 24 months from November 2012 to October 2014 among the MDR-TB patients registered under RNTCP in all the 9 Tuberculosis Units (TUs) of Krishna District, Andhra Pradesh. Inclusion Criteria being the patients who were diagnosed as MDR-TB confirmed case and those who have been initiated on treatment and registered during the above specified period. Exclusion Criteria being patients in whom death was reported and those who have opted out for private treatment or those patients who were below 14 years of age. The total number of study participants that were interviewed for were 97 and the perceptions of patients and Key staff of District TB Office, Krishna District have also been obtained regarding treatment delay. The study has obtained ethical clearance from Institutional Ethical Committee of Dr Pinnamaneni Siddhartha Institute of Medical Sciences & Research Foundation, Chinna Avutapalli, Krishna District, AP. Prior permission was obtained from State TB Officer (STO), AP and District TB Control Officer (DTCO), Krishna District, AP before the commencement of the study. Informed verbal

consent of all study subjects was taken to confirm their willingness regarding participation in the study and the data that obtained was kept highly confidential.

Case Definitions:

MDR-TB suspect: A patient suspected of drug-resistant tuberculosis, based on RNTCP criteria, for submission of specimens for drug-susceptibility testing[4]

Table 1: MDR-TB suspect criteria

MDR-TB SUSPECT CRITERIA	TYPE OF CASES TO BE INCLUDED
Criteria A	All failures of new TB cases (1A)
	Smear +ve previously treated cases who remain smear +ve at 4th month or later(2A)
	All Pulmonary TB cases who are contacts of known MDR- TB Case (3A)
Criteria B (includes Criteria A)	All smear +ve previously treated pulmonary TB cases at diagnosis (4B)
	Any smear +ve follow up result in new or previously treated cases (5B)
Criteria C(includes Criteria A & B)	All smear –ve previously treated pulmonary TB cases at diagnosis (6C)
	HIV TB co-infected cases at diagnosis (7C)

Source: RNTCP PMDT guidelines (2012)[4]

The Krishna District has adopted and following the "Criteria C" for the identification of MDR-TB suspects from October'2012.

Definition of MDR-TB Case:

A TB patient whose sputum is culture positive for *Mycobacterium tuberculosis* and is resistant *in-vitro* to isoniazid and rifampicin with or without other anti-tubercular drugs based on DST results from an RNTCP-certified Culture & Drug Susceptibility Testing (C&DST) Laboratory.

In addition to this definition, if the C&DST results of MDR-TB suspects show **"any Rifampicin resistance"**, then they should also be managed the same way as MDR-TB cases even if they do not formally qualify as MDR-TB case as per the above definition and hence, those cases have also been taken into consideration[4].

Treatment Delay: The duration between the confirmation of the MDR-TB at the C&DST laboratory and the initiation of treatment. A confirmed MDR-TB case should be started on treatment within 7 days from the date of diagnosis, beyond which, it is considered as treatment delay.

Since there was no standard definition available for treatment delay among MDR-TB patients, in the present study, we have applied the definition of treatment delay of TB cases from RNTCP Guidelines [5] and also by considering practical feasibility of treatment initiation as per the existing PMDT Guidelines (2012)[4].

Data Variables and their Source in Parenthesis are TB Registration Number(TB Register), Number of MDR-TB suspects (Line-lists from Senior TB Laboratory Supervisor (STLS)), HIV Status (Line-lists from STLS , RNTCP Referral for C & DST Register maintained at District TB Centre for diagnosis and Follow up), Number of MDR-TB suspects referred for culture and DST (RNTCP Referral for C & DST Register for diagnosis and Follow up), Number of MDR-TB suspects diagnosed as MDR-TB confirmed case

(RNTCP Referral for C & DST Register for diagnosis and Follow up) and Number of diagnosed MDR-TB cases initiated on treatment (Drug Resistant TB Register (DR-TB Register maintained at the DR-TB Centre [erstwhile Known as DOTS Plus Site] and DR-TB Treatment cards)

Piloting of the Study: In the month of October i.e., one month prior to the actual data collection period, a pilot study was conducted on a sample of 10 subjects to examine the feasibility of the questionnaire and for any incorporation that can be made in the questionnaire. Results of pilot study did not show any major alterations.

The Study Variables were broadly sub-divided into 3 groups, the first being socio demographic Variables, the second being Clinical Profile and the third being factors studied for the delay in treatment initiation of MDR-TB cases. Data Validation was done by cross checking from various records for the same variable so that record errors can be minimized. Data was entered in MS Excel 2007 and then imported to SPSS Version 20 and later analyzed by applying the descriptive statistics and Chi-square test.

Fig 1: Flow of MDR-TB patients in the current study
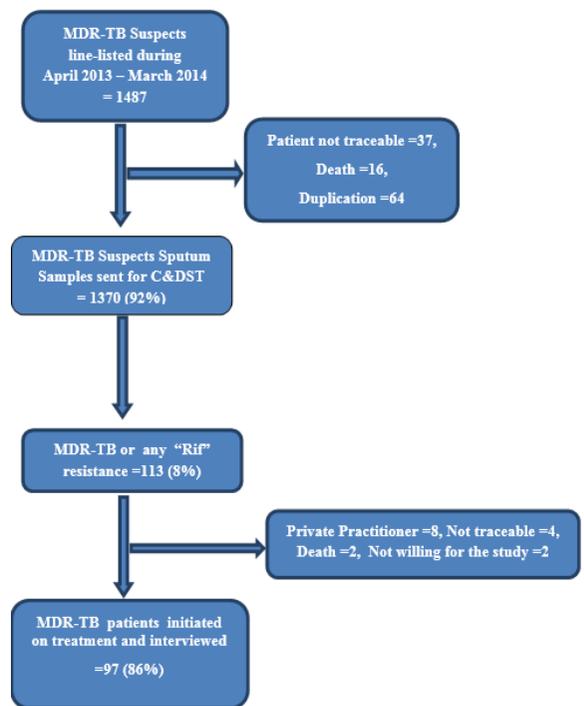
Results

Table 2. Socio-demographic factors of the study

Socio-demographic Factor	Frequency	Percentage
Gender		
Male	66	68
Female	31	32
Age	Frequency	Percentage
15-24 yrs	11	11
25-34 yrs	17	18
35-44 yrs	37	38
45-54 yrs	22	23
55-64 yrs	09	09
>65 yrs	01	01
Place of residence	Frequency	Percentage
Rural	66	68
Urban	31	32
Socio-Economic Status (SES) Scale *	Frequency	Percentage

I	05	05
II	09	09
III	32	33
IV	44	45
V	07	07
Religion	Frequency	Percentage
Christian	11	11
Hindu	79	81
Muslim	07	07
Occupation#	Frequency	Percentage
Low Skilled Workers	13	13
Unskilled Workers	34	35
Medium Skilled Workers	20	21
Unemployed	30	31
Marital Status	Frequency	Percentage
Single	06	06
Married	87	90
Widow	01	01
Divorcee	01	01
Separated	02	02
Educational Status	Frequency	Percentage
Illiterates	28	29
Primary School	41	42
Secondary School	12	12
Intermediate	06	06

Graduate	07	07
Post Graduate	03	03
Total	97	100

*SES Classification as per Modified BG Prasad SES Scale(2013), #- Occupation Classification as per SK SasiKumar et al. (2010)[6]

Among the study participants, majority (68%) were males and majority (67%) of them belong to economically productive age group "15-44 Years". Most (68%) of the MDR-TB patients belong to "rural" background and most (85%) of the study subjects belong to the lower SES (Class III, IV & V). Majority (81%) of the study subjects belong to the "Hindu Religion". About 35% of MDR-TB patients belong to "Unskilled" occupation group while 31% belong to "Unemployed" occupation group. "Medium" and "Low" Skilled occupation was present in 21% and 13% of the study subjects. None of the study subjects belong to "Highly Skilled" occupation group. Majority of the study subjects were "married" (88%) in the study and the educational status was below primary level in 71% of the study subjects while the rest (29%) had the educational status of secondary level and more than that.

Table 3: Factors responsible for treatment delay of MDR-TB Patients

Variable	Treatment Initiation		Frequency (n=97)	%	Chi-square	p-value	Inference
	≤7 Days	>7 Days					
Age							
<45 years	18	47	65	67	0.132	0.72	Not Significant
≥45 years	10	22	32	33			
Gender							
Female	08	23	31	32	0.21	0.65	Not Significant
Male	20	46	66	68			
Occupational status							
Unemployed	09	21	30	31	0.027	0.87	Not Significant
Employed	19	48	67	69			
Co-morbid condition							
Absent	24	12	36	37	39.83	<0.001	Highly Significant
Present	04	57	61	63			
Alcohol Consumption							
Absent	21	24	45	46	12.95	<0.01	Highly Significant
Present*	07	45	52	54			
Area of residence							
Rural	20	46	66	68	0.208	0.65	Not Significant
Urban	08	23	31	32			
Distance between patient's residence and DR-TB Centre							
<50 Kms	22	23	45	46	16.39	<0.001	Highly Significant
>50 Kms	06	46	52	54			
Family support							
Absent	09	53	62	64	17.23	<0.01	Highly Significant
Present	19	16	35	36			
Educational status							
Primary and below	23	46	69	71	2.32	0.12	Not Significant
Secondary and above	05	23	28	29			
Religion							
Christian	02	09	11	11			
Hindu	24	55	79	81	0.7	0.71	Not Significant
Muslim	02	05	07	08			
SES Scale#							
Lower SES (Class III,IV,V)	11	49	60	62	8.49	<0.01	Highly Significant
Upper SES (Class I & II)	17	20	37	38			
HIV Status							
Negative	25	61	86	89	0.015	0.9	Not Significant
Positive & Unknown	03	08	11	11			
Smoking Habit							
Absent	17	52	69	71	2.1	0.15	Not Significant
Present*	11	17	28	29			

*indicates current and past status, #- SES as per Modified BG Prasad Classification (2013)

The factors that were associated with treatment delay and where in that association was statistically significant were presence of co-morbid illness, alcohol consumption, lack of family support, long distance of Drug Resistant TB centre (DR-TB) centre from patient's residence and Lower Socio-Economic Status (SES)

Table 4: Reasons for the Delay in Treatment Initiation (Patient & Health System Perception)

Reasons for the delay in Treatment Initiation(Patient Perception)	Frequency*
Long distance travel	41
Lack of money	21
Lack of attendant	21
Long duration of treatment	06
Private practitioner	05
Side effects fear	05
Gender barriers	02
Exams	01
Reasons for the delay in Treatment Initiation (Health System Perception)	**Frequency***
Lack of alternate arrangement at district level for Pre-Treatment Evaluation (PTE)	39
Attendant a must	06
Proper counselling	04
Delay in tracing	02
Food not given to attendant	02
DR-TB centre staff non co-operative	01
Transferred patient not followed properly	01

*includes multiple responses

Discussion
In the present study, 87% of the study participants who had history of alcohol consumption had treatment delay and this was found to be statistically significant which was similar to the study findings of Storla DG et al (2008)[7] and Rajeswari R et al (2002)[8] Co-morbidity which was present in 93% of study participants had led to treatment delay and this association was found to be statistically significant. Co-morbidity was an independent risk variable in the study done by Jurcev-Savicevic A et al (2012)[9] and Mor Z et al (2013)[10]. Findings of the present study has shown that patients who had to travel more than 50 Kilometers (Kms) to reach DR-TB centre had experienced delay in treatment initiation compared to those who had to travel less than that. This association between long distance travel and delay in treatment initiation was found to be statistically significant and these findings are similar to the study of Makwakwa L et al (2014)[11]. There was also a recommendation by an Indian study, by Chadha SS et al (2011)[3] that DR-TB centres need to be decentralized to the district level which would decrease treatment delay of these MDR-TB patients. According to RNTCP PMDT guidelines (2012)[4] and WHO-Eastern Mediterranean Research Publication study (2006)[12], which recommended that an alternate local arrangement for Pre-Treatment Evaluation (PTE) and treatment initiation has to be considered and implemented without fail to reduce the treatment delay. In the present study, lower SES is associated with treatment delay which was also one of the important factors that was independently associated with delay in treatment initiation in the studies of Storla DG et al (2008)[7,] Rajeswari R et al (2002)[8] and Mor Z et al (2013)[10].

Reasons for treatment delay – Patients perspective:
According to the patients perspective, long distance travel remained the most important reason for delay in starting treatment, 41 responses were recorded supporting this.

This was followed by reasons like lack of money and lack of family support or attendant to accompany them to DR-TB centre, 21 responses of each were recorded on this. The other important reasons were long waiting time for PTE, approaching private practitioners and fear of side effects.

Reasons for treatment delay – Health care system perspective:
Lack of alternate arrangement for PTE at the district level is one of the important reasons for treatment delay, 39 responses were recorded on this. This is an important factor responsible for treatment initiation delay which can be addressed by the arrangement of the same at district level by District TB Control Society (DTCS).

The second important reason being lack of attendant for admission of the patients at DR-TB centre, which is a basic requirement for admitting any patient in any hospital, failing which, treatment delay occurs naturally.

The other reasons being, lack of proper counselling to the patient on importance of prompt initiation of treatment, delay in tracing the diagnosed patient by the staff, food not being provided to attendants, DR-TB centre staff not being friendly and co-operative. Lack of proper follow up on the transferred patients from one DR-TB area to the other also contributed to delay in treatment initiation.

Conclusion
The factors responsible for the delay in treatment initiation were co-morbid illness, alcoholism, lack of family support, long distance of Drug Resistant Tuberculosis centre (DR-TB centre) from patient's residence and low monthly per capita income (lower SES).

The first *Limitation* of the study was that the small sample size of the present study would have resulted in statistically non significant association with some of the important variables such as smoking, gender, marital status, HIV infection and occupation; Second *limitation* was that the perceptions of the study participants regarding the reasons for the treatment delay if collected using open ended questionnaire and analysed using *complete qualitative methodology* would have explored the reasons in depth.

Recommendations:
Decentralization of Drug Resistant TB Centre (DR-TB Centre) at the district level would result in earlier initiation of treatment, recruitment of Key staff immediately as and when vacancies arise, health education to patients to adopt a healthy life style to abstain them from harmful risk factor like alcoholism and linking the TB programme to relevant services for co-morbid conditions, sensitization of private practitioners for early identification followed by referral of MDR-TB suspects for early diagnosis of MDR-TB cases and their timely treatment initiation would decrease the treatment delay.

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