International Journal of Community Medicine and Public Health
Shameer KM et al. Int J Community Med Public Health. 2016 Apr;3(4):962-967
http://www.ijcmph.com
pISSN 2394-6032 | eISSN 2394-6040

DOI: http://dx.doi.org/10.18203/2394-6040.ijcmph20160937

Research Article

A community based case control study on risk factors for treatment interruptions in people with tuberculosis in Kollam district, Kerala, southern India

Shameer K. M.[1], Manjunath K.[1], Sam D. Marconi[1], Krishnaveni V.[2], Rakesh P. S.[3]*, Jasmin H. Prasad[1]

[1]Department of Community Health, Christian Medical College, Vellore, Tamil Nadu, India
[2]District TB Centre, Kollam, Kerala, India
[3]Centre for Public Health Protection, Kollam, Kerala, India

Received: 12 February 2016
Accepted: 08 March 2016

***Correspondence:**
Dr. Rakesh P. S.,
E-mail: rakeshrenjini@gmail.com

ABSTRACT

Background: Treatment adherence to anti-TB treatment is a critical determinant of treatment outcomes, prognosis and further emergence of drug resistance. The objective of the study was to identify the risk factors for treatment interruptions among the newly diagnosed patients with tuberculosis registered for treatment under Revised National Tuberculosis Control Program in Kollam District, Kerala, southern India.
Methods: A community based case control study was undertaken with cases being patients registered for TB treatment under category I in two randomly selected TB Units of Kollam districts with 'treatment interruption' as defined by missing at least three consecutive doses of anti TB medicines. Controls were those who successfully completed the anti-tuberculosis treatment regimen. Interview was conducted with a structured questionnaire. Univariate and multivariate analysis was done and odds ratios with 95% confidence interval for the risk factors for treatment interruption were calculated.
Results: A total of 47 cases and 94 controls were interviewed. In the final logistic regression model, hazardous alcohol use (Adjusted OR 16.67, 95% CI 3.22-61.42) and adverse drug reactions (Adjusted OR 2.46, 95% CI 1.07-6.14) were found as statistically significant risk factors for treatment interruption.
Conclusions: Hazardous use of alcohol and adverse effects to drugs are identified as the potential risk factors for treatment interruptions among the people with TB initiated on Category 1 DOTS regimen in Kollam district, Kerala, India. Alcohol use disorder and hazardous drinking among TB patients is a matter of concern that needs to be translated to an effective intervention program.

Keywords: Alcohol, DOTS, Treatment adherence, Treatment interruption, Tuberculosis

INTRODUCTION

India remains to be a high burden TB country contributing to 23% of all TB cases in the World.[1] The incidence, prevalence and mortality rates of TB disease in the country were 167, 195 and 17 per 100000 population. Drug-resistant TB also poses a major threat to control of TB in the country. India notified more than 25000 Multi Drug Resistance TB cases in 2014.[1]

Adherence to regular and complete treatment is one of the important factors for relapse free cure from TB.[2] Treatment adherence is also a critical determinant of treatment outcomes, prognosis and further emergence of drug resistance.[2-4] If untreated, the confirmed TB cases are the potential source for spreading the infection in the community and inside the house hold.

Morbidity of illness, financial burden, access issues, social stigma, confidentiality issues and adverse reactions

to drugs often makes TB care a complex issue and these factors often determine patient's adherence to TB treatment.[5,6] The Directly Observed Short course Strategy (DOTS) using a thrice weekly regimen for six months has been the backbone of country's TB programmes for last two decades. The Direct Observation of Treatment (DOT) is an important component of the strategy and is an attempt to improve adherence by active monitoring and recording of the consumption of each and every drug dose by an 'observer' acceptable to the patient and the health system.

Kerala, the southernmost state in India, has achieved near universal literacy and many of the maternal and child health indicators comparable to countries with more advanced economies. Health coverage indicators of the state are promising. Health seeking and access to service are high.[7] Kerala is implementing RNTCP since 1998. It is estimated to have a relatively low TB burden compared to other parts of the country.[8] Despite the strong administrative and interventional strategies by Government and other various agencies, in Kerala, the lost to follow up rate for new smear positive (NSP) cases was five percent and which is constant over the years.

The objective of the study was to identify the risk factors for treatment interruptions among the newly diagnosed patients with tuberculosis registered for treatment under category I of RNTCP (Revised National Tuberculosis Control Program) in Kollam District. The results of this study would help the policy makers and the program managers to understand the reasons for treatment interruptions and to tailor the treatment support mechanism to people with TB in ensuring adherence in Kerala State.

METHODS

Kollam district, located in the south west cost of Kerala has a population of 2.6 million. Kollam district represents the state in terrain, population characteristics and health care service delivery. The district examined 278 presumptive TB cases and had notified 38 new smear positive cases per 10000 populations in 2014.

A community based case control study was undertaken with cases being patients registered for TB treatment under category I in two (out of five) randomly selected TB Units of Kollam districts from October 2014 to June 2015 (4th quarter 2014 to 3rd quarter 2015), with 'treatment interruption' as defined by missing at least three consecutive doses of anti TB medicines. Controls were randomly selected from the list of patients registered for TB treatment under Category I in the same TUs during October 2014 to June 2015 and who successfully completed the anti-tuberculosis treatment regimen for specified period of time without any documented treatment interruptions. Patients who were 'transferred out' or 'transferred in' from other districts or States and patients who were not on DOT under RNTCP were not included in the study.

With two controls per cases, an alpha error of 5%, power of 80 %, an anticipated odds ratio of 2.5 and the proportions of controls with hazard alcoholism as 20%, the sample size was calculated as 40 cases and 80 controls. An additional 20% was added to the sample size to deal with non-response.

Training was given to all Multi- purpose health workers of the study area to immediately report anybody on Category I TB treatment that missed three consecutive doses of anti TB medications. DOT providers of the area were sensitised for the same. The investigators visited the primary health centres of the area fortnightly and verified all TB treatment cards to identify cases. The multipurpose workers, DOT providers and Senior Treatment Supervisors used to do 'default retrieval' actions as routine.

Data was collected by interviewing the cases and controls by the Principal Investigator at their houses, using a structured questionnaire. The questionnaire was developed based on literature review, group consensus and expert opinions. The questionnaire was translated to local language (Malayalam) and was back translated to check for consistency. It was pilot tested before use. Each interview lasted for about 30 minutes. Precautions were taken to ensure privacy during the interview. The study protocol was approved by the Institutional Review Board of Christian Medical College, Vellore. A verbal consent was obtained before visiting patient's house. A written informed consent was obtained by the investigator by visiting the patient's home.

Questionnaire included the demographic details, adverse drug reactions, social and family support (disclosed TB status with family members, most supporting person during treatment period, support from the family member towards treatment), personal habits of participants (tobacco, alcohol, substance abuse) , factors related to health system (selection of DOT provider, convenience, distance to nearest Peripheral Health Institutions, initial counselling, conflicts with DOT provider), social stigma perceived by patients (social stigma scale used by the World Health Organisation for a study among TB patients)[9] and details of alcohol use. The Alcohol Use Disorders Identification Test (AUDIT) Questionnaire was used to classify drinking habits and a cut off score of 8 or above was considered as hazardous drinking.[10] Variables measuring stigma were recorded on a 5-point Liker t scale (0 the highest and 4 the lowest degree of stigma). These variables included: feeling ashamed of having tuberculosis; having to hide tuberculosis diagnosis from others; cost incurred by the long disease duration; isolation due to tuberculosis; able to decide about getting tuberculosis treatment, and the extent to which tuberculosis affects the following: relation with others; work performance; marital relations; family

responsibilities; chances of marriage; family relations. Socio Economic Status was assessed by modified Kuppuswamy's scale which considered income, education and occupation.[11]Possible adverse drug reactions of anti- TB drugs as experienced by patients were recorded.

Data entry was done using Epi Info 3.5.1 and data was analyzed using Statistical Package for Social Sciences version 15 (SPSS Inc., Chicago, IL, USA), for Microsoft Windows. Chi square test was used to test difference between proportions. The stigma score was calculated according to guidelines and was categorised taking median of controls as the cut off.[9] Univariate analysis was done to generate an odds ratio and 95% confidence interval for the risk factors for treatment interruption. Risk factors with p values <0.1 along with age and gender were included in the multivariate analysis in a back ward conditional step wise logistic regression model.

RESULTS

During the study period there were a total of 782 patients initiated on category I anti TB treatment under RNTCP in the study area. Of the 50 patient who interrupted the treatment (missed at least three doses) during the study period, two of them moved out of the area and one did not give consent to participate in the study. Thus a total of 47 cases and 94 controls were interviewed.

In the study, 51.1% of cases and 63.8% of controls were above 45 years of age (p 0.151). Among those who interrupted, 38.3% had lower than primary education while the figure was 14.9% among controls (OR 3.54, 95% CI 1.56-8.03). Socio demographic characteristics of the study subjects were shown in Table 1.

Among the cases 80.9% had pulmonary TB while 75.5% among the controls had the same (p 0.521). Adverse drug reactions were reported by 55.3% of cases and 29.8% of controls (OR 2.91, 95% CI 1.41-6.02). Distance to the nearest peripheral health institution was more than two kilo meters for 83% of cases and 63.8% of controls (OR 2.76, 95% CI 1.15-6.58). Details of disease condition, co-morbidity, adverse drug reactions and health system related factors were shown in Table 2.

Table 1: Socio demographic characteristics of the study participants.

Characteristics	Category	Cases (N=47)	Controls (N=97)	p-value	Odds ratio (95% CI)
Age	<45 years	23 (48.9%)	34 (36.2%)	0.151	1.69 (0.83-3.4)
	>45 years	24 (51.1%)	60 (63.8%)		
Gender	Male	38 (80.9%)	69 (73.4%)	0.332	1.53 (0.67-3.70)
	Female	9 (19.%1)	25 (26.6%)		
Education	Up to Primary School	18 (38.3%)	14 (14.9%)	0.003	3.54 (1.56-8.03)
	Above primary school	29 (61.7%)	80 (85.1%)		
Occupation	Nil/Unskilled	9 (19.1%)	21 (22.3%)	0.821	0.82 (0.34-1.97)
	Others	38 (80.9%)	73 (77.7%)		
Socio-Economic Status	Lower	43 (91.5%)	75 (79.8%)	0.094	2.72 (0.87-8.5)
	Middle	4 (8.5%)	19 (20.2%)		

Table 2: Details of disease condition, adverse drug reactions and health system related factors.

Characteristics	Category	Cases (N=47)	Controls (N=94)	p value	Odds ratio (95% CI)
Type of TB	Pulmonary	38 (80.9%)	71 (75.5%)	0.521	1.36 (0.57-3.25)
	Extra pulmonary TB	9 (19.1.0%)	23 (24.5%)		
Adverse drug reactions	Present	26 (55.3%)	28 (29.8%)	0.006	2.91 (1.41- 6.02)
	Absent	21 (44.7%)	66 (70.2%)		
Initial counselling	Received	44 (93.6%)	88 (93.6%)	1.00	1.00 (0.23-4.18)
	Not received	3 (6.4%)	6 (6.4%)		
Selection of DOT centre after consulting with patient	No	5 (10.6%)	4 (4.3%)	0.161	2.67 (0.68-10.48)
	Yes	42 (89.4%)	90 (95.7%)		
Any Conflict with DOT provider	Yes	8 (17.0%)	8 (8.5%)	0.167	2.20 (0.77-6.30)
	No	39 (83%)	86 (91.5%)		
Distance to nearest PHI	>2 KM	39 (83%)	60 (63.8%)	0.020	2.76 (1.15-6.58)
	<=2 KM	8 (17.0)	34 (36.2%)		

Table 3: Factors related to substance abuse, family support and social stigma.

Characteristics	Category	Cases (n=47)	Controls (N=94)	p-value	Odds ratio (95% CI)
Current Smoker	Yes	15 (31.9%)	5 (5.3%)	<0.001	8.34 (2.80-24.81)
	No	32 (68.1%)	89 (94.7%)		
Alcohol	Never used	13 (27.7%)	52 (55.3%)		1
	Non-hazardous use	17 (36.2%)	39 (41.5%)	0.211	1.74 (0.75-4.01)
	Hazardous use	17 (36.2%)	3 (3.2%)	<0.001	22.67 (5.76- 89.16)
Shared TB Status with Family	No Yes	10 (21.3%) 37 (78.7%)	8 (8.5%) 86 (91.5%)	0.058	2.90 (1.06-7.94)
Family Support	Yes No	39 (83%) 8 (17%)	83 (88.3%) 11 (11.7%)	0.431	0.64 (0.24-1.73)
TB Stigma perceived by the patient	Higher degree Lower degree	35 (74.5%) 12 (25.5%)	46 (48.9%) 48 (51.1%)	0.004	3.04 (1.40-6.51)

In the study, 31.9% of cases and 5.3% of controls were current smokers (OR 8.34, 95% CI 2.80-24.81) and 36.2% of cases and 3.2% of controls were hazardous alcoholic users (OR 22.67, 95% CI 5.76- 89.16). A higher social stigma was perceived by 74.5% of cases and 48.9% of the controls (OR 3.04, 95% CI 1.40-6.51). Details of factors related to substance abuse, family support and social stigma were as shown in Table 3.

In the final logistic regression model, hazardous alcohol use (Adjusted OR 16.67, 95% CI 3.22-61.42) and adverse drug reactions (Adjusted OR 2.46, 95% CI 1.07-6.14) were found as risk factors for treatment interruption. The final logistic regression model was as shown in Table 4.

Table 4: Logistic regression model for factors associated with treatment interruption.

Characteristics	Adjusted odds ratio	95% CI
Education (lower)	2.25	(0.83-6.13)
Socio-economic Status (lower)	1.02	(0.25-4.07)
Adverse drug reactions (Yes)	2.46	(1.07-6.14)*
Distance to nearest PHI (>2 KM)	2.99	(0.99-8.99)
Alcohol (hazardous use)	16.67	(3.22-61.42)*
Current smoker (Yes)	3.84	(0.92-16.06)
Presence of social stigma (Yes)	2.65	(1.00-7.01)
Shared treatment status with family (Yes)	2.22	(0.52-9.50)

*p<0.05

DISCUSSION

Standards of TB care in India (STCI) and the End TB strategy emphasised the importance of a patient-centred approach to foster adherence. It has also been laid down in STCI that treatment adherence goes beyond the realm of DOTS. This case control study aimed at identifying the risk factors for treatment interruptions among people initiated on TB treatment within the DOTS strategy in Kerala. Treatment interruption was considered in this study when a patient missed three doses of medicines consecutively, as this would be an early signal for 'defaulting' treatment.

Harmful Alcohol use by the patients was identified to be the major risk factor for treatment interruptions. The finding is consistent with results from many studies from various parts of the country and abroad.[12-16] Alcoholism is a serious public health problem and a challenge for the tuberculosis control program in south India.[17]

Incorporating a qualitative design would have helped in answering why is hazardous alcohol use associated with treatment interruptions. Those with hazardous drinking might choose not to turn up for treatment as they may be worried about adverse effects of medicines taken with alcohol. It could also be because that health being a 'low priority' issues for them. Primary health care team and the RNTCP team in Kerala, used to report 'alcoholism' as the major reasons for 'default' and as the major factor for unsuccessful default retrieval actions. The capacity of the primary care team and TB Control team to deal with alcoholism has to be build.

Alcohol consumption rates are higher in Kerala as compared to other States in India. Hazardous drinking among TB patients is a matter of concern for the State that needs to be translated to an effective public health intervention program.[18] Eliciting the history of alcoholism prior to anti- TB treatment initiation would help in identifying those who are potential defaulters at the beginning itself. Improving treatment compliance among alcoholic patients through support from family, health staff and social organizations will be challenging. However social inclusion model from Pathanamthitta district, Kerala, with incorporation of a "Treatment Support Group" which is a non-statutory body of socially responsible citizens and volunteers to provide social support to each needy TB patient safeguarding their

dignity and confidentiality by ensuring access to social welfare programs, empowering the patient for making decision to complete treatment successfully, has reduced the lost to follow up rates to near zero among new smear positive cases.[19] Is this strategy useful for dealing with lost to follow up among hazardous alcoholic users in other areas need to be experimented.

There is no formal intervention in place in the country for TB patients with hazardous alcohol use. A study from Russia reported successful introduction of the AUDIT to screen TB patients for alcohol use disorder, established referral algorithms, and hired additional staff to integrate alcohol use disorders management in TB services.[20,21] A recent study that assessed the feasibility of integrated alcoholism–tuberculosis treatment and care suggested the immediate need in India.[22]

Adverse Drug Reactions (ADR) is known risk factors for treatment interruption and default from TB treatment.[23-25] Frequently reported minor side effects could be dealt with proper instructions on drug consumption, reassurance to patients and prompt symptomatic treatment before it leads to default.

The study could not identify any health system related factors as the risk factors for treatment interruption. This could be due to the well-functioning integrated RNTCP activities with a comparatively stronger general health system in place. It could also be due to the lack of power due to a smaller sample size to study many of the possible risk factors. The presence of alcoholism as a strong risk factor would have masked the effects of other factors during the multivariate analysis.

Recall, reporting and interviewer bias would have affected the study results. We have taken all possible measures to avoid the bias. The information was collected by the investigator using a structured questionnaire and the interview techniques were standardised. We were prospectively following the TB cohort to identify treatment interruptions at the earliest and interview was conducted at the earliest possible dates. This would have minimised the recall bias. The element of bias involved with self-reported information, especially on alcohol use cannot be ruled out. Residual confounding may remain. The study was under powered due to smaller sample size to study many of the risk factors including social stigma. Being done in a community based setting, robust and validated tools used for interviews and the designs itself are the strengths of the study.

CONCLUSION

To summarise, hazardous use of alcohol to a major extent and adverse effects to drugs to some extent are identified as the potential risk factors for treatment interruptions among the people with TB initiated on Category 1 DOTS regimen in Kollam district, Kerala, India. Alcohol use disorder and hazardous drinking among TB patients is a matter of concern that needs to be translated to an effective intervention program.

ACKNOWLEDGEMENT

Dr Shibu Balakrishnan, WHO Consultant (TB), Dr Aneesh Junior consultant, DTC Kollam. Senior Treatment supervisors, TB Health Visitors , lab staffs , Medical Officers and Multipurpose health workers at Primary Health Centres and DOT providers of Kollam district.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. World Health Organisation. Global Tuberculosis Report.Geneva. WHO. 2015
2. Burman WJ, Cohn DL, Rietmeijer CA, Judson FN, Sbarbaro JA, Reves RR. Nonadherence with directly observed therapy for tuberculosis. Epidemiology and effect on the outcome of treatment. Chest. 1997;111:1168-73.
3. Paramasivan CN, Venkataraman P. Drug resistance in tuberculosis in India. Indian J Med Res. 2004;120:377-86.
4. Babiarz KS, Suen S, Goldhaber-Fiebert JD. Tuberculosis treatment discontinuation and symptom persistence: an observational study of Bihar, India's public care system covering >100,000,000 inhabitants. BMC Public Health. 2014;14:418.
5. Vijay S, Kumar P, Chauhan LS, Vollepore BH, Kizhakkethil UP, Rao SG. Risk Factors Associated with Default among New Smear Positive TB Patients Treated Under DOTS in India. Pai M, ed. PLoS ONE. 2010;5(4):e10043.
6. Sarpal SS, Goel NK, Kumar D, Janmeja AK. Reasons for interruption of anti-tubercular treatment among the retreatment patients in category II of RNTCP in Chandigarh, north India. Indian J Tuberc. 2014;61(2):121-8.
7. Thankappan KR, Valiathan MS. Health at low cost-the Kerala model. The Lancet. 1998;351:1274-5.
8. Kumar S, Radhakrishna, Chadha VK. Prevalence of tuberculous infection among school children in Kerala. Indian J Tuberc. 2009;56:10-16.
9. World Health Organisation. The Alcohol Use Disorders Identification Test. Guidelines for Use in Primary Care. WHO. Geneva. 2001.
10. World Health Organisation. Diagnostic and treatment delays in Tuberculosis. WHO. 2006. WHO-EM/TDR/009/E
11. Oberoi S. Updating income ranges for Kuppuswamy's socio-economic status scale for the

year 2014. Indian J of Pub Health. 2015;59(2):156-7.
12. Santha T, Garg R, Frieden TR, Chandrasekaran V, Subramani R. Risk factors associated with default, failure and death among tuberculosis patients treated in a DOTS programme in Tiruvallur District, south India. Int J Tuberc Lung Dis. 2000;6:780-8.
13. Vijay S, Balasangameshwara VH, Jagannatha PS, Saroja VN, Kumar P. Defaults among Tuberculosis Patients treated under DOTS in Bangalore City- A search for solution. Indian J Tub. 2003;50:185-95.
14. Jakubowiak WM, Bogorodskaya EM, Borisov ES, Danilova DI, Kourbatova EK. Risk factorsassociated with default among new pulmonary TB patients and social support in six Russian regions. IntJ Tuberc Lung Dis. 2007;11:46-53.
15. PinidiyaPathirage J, Senaratne W, Wickremasinghe R. Prevalence and predictors of default with tuberculosis treatment in Sri Lanka. Southeast Asian J Trop Med Public Health. 2008;39:1076-82.
16. Muture BN, Keraka MN, Kimuu PK, Kabiru EW, Ombeka VO, Oguya F. Factors associated withdefault from treatment among tuberculosis patients in Nairobi province, Kenya: A case control study. BMC Public Health. 2011;11:696-700.
17. Suhadev M, Thomas BE, M RS, PM, VC. Alcohol Use Disorders (AUD) among Tuberculosis Patients: A Study from Chennai, South India. PLoS ONE. 2011;6(5):e194.
18. Sugathan TN, Soman CR, Sankaranarayanan K. Behavioural risk factors for non-communicable diseases among adults in Kerala, India. Indian J Med Res. 2008;127:555-63.
19. Balakrishnan S, Manikantan J, Sreenivas A, Jayasankar S, Sunilkumar M, Rakesh PS. Social inclusion: An effort to end loss-to-treatment follow-up in tuberculosis. Indian Journal of Tuberculosis. 2016.
20. Greenfield SF, Shields A, Connery HS, Livchits V, Yanov SA, Lastimoso CS, et al. Integrated management of physician-delivered alcohol care for tuberculosis patients: design and implementation. Alcohol Clin Exp Res. 2010;34:317-30.
21. Shin S, Livchits V, Connery HS, Shields A, Yanov S, Yanova G, et al. Tomsk Tuberculosis Alcohol Working Group Effectiveness of alcohol treatment interventions integrated into routine tuberculosis care in Tomsk, Russia. Addiction. 2013;108:1387-96.
22. Thomas B, Suhadev M, Mani J, Ganapathy BG, Armugam A, Faizunnisha F, et al. Feasibility of an alcohol intervention programme for TB patients with alcohol use disorder (AUD)-a qualitative study from Chennai, South India. PLoS ONE. 2011;6:e27752.
23. Chang KC, Leung CC, Tam CM. Risk factors for defaulting from anti-tuberculosis treatment under directly observed treatment in Hong Kong. Int J Tuberc Lung Dis. 2004;8(12):1492-98.
24. Tekle B, Mariam DH, Ali A. Defaulting from DOTs and its determinants in three district of Arsi Zone in Ethiopia. Int J Tuberc Lung Dis. 2002;6:573.
25. Comolet TM, Rakotomalata R. Factors determining compliance with tuberculosis treatment in an urban environment, Tamatare, Madagascar. Int J Tuberc Lung Dis. 1998;2:891-7.

Cite this article as: Shameer KM, Manjunath K, Marconi SD, Krishnaveni V, Rakesh PS, Prasad JH. A community based case control study on risk factors for treatment interruptions in people with tuberculosis in Kollam district, Kerala, southern India. Int J Community Med Public Health 2016;3:962-7.