International Journal of Health Sciences and Research
www.ijhsr.org ISSN: 2249-9571

Original Research Article

Risk Factors for Unfavourable Fate Cases after Two Years of Directly Observed Treatment Short Course Chemotherapy (DOTS)

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Received: 05/03//2014 *Revised: 01/04/2014* *Accepted: 07/04/2014*

ABSTRACT

Background: Change in disease status over a period of time is termed as fate. During a non-intervention period, the fate of cases reflects the natural dynamics of the disease. The fate may be favourable as free from disease and unfavourable as death / bacteriologically positive.
Objective: To identify the risk factors for unfavourable fate cases after two years of DOTS.
Methodology: The present cross section study was carried out on TB cases which were registered for DOTS in 2006. The cases were distributed into various strata by Stratified Random Sampling method and to get the representation of each type of TB cases, cases were chosen by Systematic Random Sampling Method from each stratum. Out of 357, total 304 cases were contacted.
Results: Out of total 304, 254 (83.55%) cases had favourable fate and 50 (16.45%) unfavourable. After two years of DOTS Chemotherapy, four cases found bacteriologically sputum positive and six previous sputum negative/ extra-pulmonary cases had relapsed with clinical and histological evidence of current active TB. The relapse rate was 0.99% (3/304). The set of variables which determines the prediction model for increased risk of unfavorable cases were age above 35 years, married, illiteracy, past history of TB and first actions at government institutes.
Conclusion: This study may add the knowledge on TB, time trend for mortality and natural dynamic of TB disease. The risk factors derived by logistic regression applied to identify lacunae/ obstacles due to which patients land up in unfavourable fate.

Key words: Tuberculosis, DOTS, Favourable fate, Unfavourable fate.

INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by Mycobacterium TB.TB remains a world-wide public health problem despite the fact that the causative organism was discovered more than 100 years ago and highly effective drugs and vaccine are available making TB a preventable and curable disease. [1] It reduces the working capacity of infected persons and extracts a heavy toll from families and the country as a whole. Hence it is a disease with devastating social and economic costs. [2]

Relapse after treatment is a crucial determinant of relative merits of chemotherapeutic regimens. Majority of relapses after Short Course of Chemotherapy (SCC) occur within two years after treatment initiation. [3] Change in disease status over a period of time is termed as "fate". The disease status may have been classified as cure, continued to be suspect case, converted into bacillary cases and dead. [4] The fate may be favourable as free from disease and unfavourable as death / bacteriologically positive. [5]

The sociological problems were faced by the patients following their treatment. It becomes necessary to investigate the behaviour of a patient with respect to his efforts to cope with the changed situation following prolonged sufferings, as are the treatment results in terms of deaths, bacteriological conversion and emergence of drug resistance. [4]

There are very few studies regarding the fate or long-term follow up of TB patients after DOTS. Also, information related to their socio-economic profile and risk factors associated with relapse, default and mortality is little known. Hence the present study regarding the fate of TB patients after two years of DOTS treatment has been undertaken. Reasons or risk factors can be related to Patient, Health System, Drugs and Others social problems.

Objective: To identify the risk factors for unfavourable fate cases after two years of DOTS.

MATERIALS AND METHODS

Selection and Description of Participants:

The present cross section study was carried out on TB cases which were registered for DOTS in 2006. The lists of all TB cases registered in two Tuberculosis Units were obtained from City TB Officer (CTO). This study was conducted in Aurangabad city Municipal Corporation area during the period of October 2009 to September 2010. The February 2001 was the first year of implementation of RNTCP in Aurangabad city Out of 1096 registered cases, 395 TB cases were NSP cases. The TB cases registered for DOTS in 2006 year were taken as study population.

Sampling technique: The cases were distributed into various strata by Stratified Random Sampling method according to RNTCP guidelines such as New Sputum Positive (NSP), New Sputum Negative (NSN), New Extra pulmonary (NEP) and Treatment after Default (TAD), Failure, Relapse and Other. Out of 1096, the 32 cases were transferred out and would not be available for interview, hence excluded. Thus, the study population became 1064. Taking into consideration of feasibility and time required to gather data, it was decided to take 1/3rd of the study population. Further to get the representation of each type of TB cases, cases were chosen by Systematic Random Sampling Method from each stratum.

Sample size: The cases which were not found at their residence despite three visits were labeled as 'not traceable'. Out of 357, total 304 cases were contacted and remaining 53 cases remained not traceable. So the sample size became 304.

Technical Information:

The investigator prepared an address list of the cases from TB Register. The TB Cases were followed up with help of DOT providers and interviewed at their residence using a predesigned and pretested proforma after taking their consent. The data regarding socio-demographic and environmental risk factors was collected. The information regarding survival status of TB cases was collected. If TB cases found dead, time and cause of death were ascertained from relatives and/ or neighbourhood. The symptomatic cases were evaluated bacteriologically.

Table no. 1. The selection of TB cases from TB Register.

Type of cases	No. of cases by Stratified Random Sampling	No. of cases after exclusion of transferred out	No. of TB cases by SRS Method	Study cases
NSP	395	382	128	108
NSN	177	172	58	51
NEP	306	300	100	82
TAD	51	50	17	14
Failure	8	8	3	2
Relapse	86	81	27	24
Other	73	71	24	23
Total	1096	1064	357	304

(Source: City Tuberculosis Officer, RNTCP TB Register, Aurangabad)

The fate of TB cases was described in terms of favourable and unfavourable status. Bacteriologically negative and free from TB disease were labeled as favourable fate. The bacteriologically positive, other type and death cases were included in unfavourable fate.

Statistics:

The information was interpreted in terms of percentages, Crude odds ratio (OR), 95% confidence intervals (CI) and Chi square tests. Statistical significance was set at P value of less than or equal to 0.05. The distribution of potential risk factors was assessed among favourable fate and unfavourable fate. Univariate analysis was performed using Epi-Info version 3.5.1 (Centers for Disease Control, Atlanta, GA, 2001). To identify the independent association of risk factors with unfavourable fate adjusting for confounding factors, adjusted odds ratio (AOR) and 95% CI was calculated by stepwise logistic regression analysis. Multivariate analysis was performed by using Statistical Package for Social Sciences (SPSS), version 19.0.0, 2010 SPSS, Inc., an IBM company. The criteria for inclusion of variables in the model was set at $p<0.1$ and for removal $p>0.5$.

The unfavourable fate was found in11 (6.05%) cases below 35 years of age and 38 (31.71%) cases above 35 years of age. It was found that statically more number of females (116) had significantly favourable fate than males ($\chi^2= 6.62$, $p<0.05$). The unfavourable fate in Hindu

RESULTS

Out of total 304, 254 (83.55%) cases had favourable fate and 50 (16.45%) unfavourable. Of40 died cases, 12 (30%) cases had died during DOTS and 28 (70%) died after completion of DOTS treatment. After two years of DOTS Chemotherapy, four cases found bacteriologically sputum positive and six previous sputum negative or extra-pulmonary cases had relapsed with clinical and histological evidence of current active TB. Among bacteriologically positive sputum cases, two cases were previously cured outcome, one previously TC and one previously defaulted case. Thus the relapse rate was 0.99% (3/304).

TB cases was 25 (17.48%), in Muslim TB cases 10 (10.53%) unfavourable and 15 (23.08%) in Buddha religion cases. There was no significant diffrence in the fate of TB cases between Hindu and other religion ($\chi^2= 0.21$, $p >0.05$).

Table No. 2. Socio-demographic Risk factors for unfavourable fate.

Socio-demographic Risk factors		Unfavourable n=50 No. (%)	Favourable n=254 No. (%)	Odds Ratio (95% Confidence Interval)	p value
Age (years)	Below 35	11 (6.08)	170 (93.92)	1	
	Above 35	39 (31.71)	84 (68.29)	0.14(0.07- 0.29)	<0.05
Sex	Male	37 (21.14)	138 (78.86)	2.39(1.21- 4.76)	0.01
	Female	13 (10.08)	116 (89.92)	1	
Religion	Hindu	25 (17.48)	118 (82.52)	1.15 (0.63-2.11)	0.65
	Other	25 (15.53)	136 (84.47)	1	
Marital status	Unmarried	4 (8.89)	41 (91.11)	1	
	Married	46 (17.76)	213 (82.24)	0.45 (0.15-1.32)	0.14
Education	Illiterate	27 (27.27)	72 (72.73)	2.97(1.60- 5.51)	<0.05
	Literate	23 (11.22)	182 (88.78)	1	
Occupation	Unemployed	30 (18.75)	129 (80.63)	1.45(0.78- 2.69)	0.23
	Employed	20 (13.79)	125 (86.21)	1	
Type of family	Nuclear	13 (13.27)	85 (86.73)	1	
	Other	37 (17.96)	169 (82.04)	1.43 (0.72-2.84)	0.30
SES	Upper	6 (13.33)	39 (86.67)	1	
	Lower	44 (16.99)	215 (83.01)	1.33(0.53- 3.33)	0.54

Of 246 (80.92%) married individuals, the fate of 38 (15.45%) cases was unfavourable. 4 (8.89%) unmarried individuals fate was unfavourable. There was no significant difference in fate of TB cases between married and unmarried (χ^2= 2.20, p>0.05). The fate of 99 illiterate cases was 72 (77.78%) favourable and 27 (22.22%) unfavourable. The proportion of unfavourable fate in illiterate cases was significantly more than literate cases (χ^2 = 12.52, p <0.001).

The fate of total 160 (52.63%) unemployed cases was 129 (80.63%) favourable and 30 (18.75%) unfavourable. Highest numbers of unfavourable cases were found in joint family (34) followed by 13 in nuclear and only 3 cases in joint family. Chi square test had shown no significant difference in fate of TB cases with regards to employment and type of families (p values >0.05).The higher unfavourable cases were found in lower socio-economic strata i.e. 44 (16.99%).

Table No. 3. Environmental Risk factors for unfavourable fate.

Environmental Risk factors		Unfavourable n=50 No. (%)	Favourable n=254 No. (%)	Odds Ratio (95% Confidence Interval)	p value
Smoking	Yes	26 (30.95)	58 (69.05)	3.66(1.96- 6.86)	<0.01
	No	24 (10.91)	196 (89.09)	1	
Alcoholic	Yes	17 (25.76)	49 (74.24)	2.16(1.11- 4.18)	0.02
	No	33 (13.87)	205 (86.13)	1	
House	Kaccha	39 (20.42)	152 (79.58)	2.38(1.16- 4.86)	0.02
	Paccha	11 (9.73)	102 (90.27)	1	
Over-crowding	Yes	32 (17.39)	152 (82.61)	1.19(0.64- 2.24)	0.58
	No	18 (15.00)	102 (85.00)	1	
Cross ventilation	Yes	20 (13.25)	131 (86.75)	1	
	No	30 (19.61)	123 (80.39)	1.60(0.86- 2.96)	0.13
Premises hygiene	Unsatisfactory	40 (21.05)	150 (78.95)	2.77 (1.33-5.80)	0.01
	Satisfactory	10 (8.77)	104 (91.23)	1	

In this study, 26 (30.95%) cases with smoking habit were found unfavourabe fate. Type of house as paccha was more significantly associated with favourable fate than kaccha house, p<0.05. In unsatisfactory surroundings, there was increased risk of unfavourable fate. The variables such as overcrowding and cross ventilation were not significantly associated with unfavourable fate (p values >0.05).Thus, among

environment related variables smoking, alcohol drinking, type of house and premise hygiene were significantly associated with unfavourable fate.

Table No. 4. TB Disease related Risk factors for unfavourable fate.

TB Disease related Risk factors		Unfavourable n=50 No. (%)	Favourable n=254 No. (%)	Odds Ratio (95% Confidence Interval)	p value
Lesion	Pulmonary	39 (18.48)	172 (81.52)	1.69 (0.82- 3.47)	0.15
	Extra-pulmonary	11 (11.83)	82 (88.17)	1	
Type of patient	New cases	38(15.70)	204(84.30)	1	
	Retreatment	12 (19.35)	50 (80.65)	0.78 (0.38-1.59)	0.48
Past Ho TB	Yes	18 (18.23)	45 (71.43)	2.61 (1.35- 5.06)	<0.05
	No	32 (13.28)	209 (86.72)	1	
Ho contact	Yes	33 (18.23)	148 (81.77)	1.39 (0.73- 2.63)	0.31
	No	17 (13.82)	106 (86.18)	1	
Delay	<4weeks	32 (24.24)	109 (82.58)	1.58 (0.89- 2.79)	0.12
	>4weeks	27 (15.70)	145 (84.30)	1	
First action at	Government	44 (22.11)	155 (77.89)	4.68 (1.92- 11.4)	<0.05
	Private	6 (5.71)	99 (94.29)	1	

It was found that 39 (18.48%) pulmonary type of TB lesion cases had unfavourable fate and 11 (11.83%) extra-pulmonary lesion. The unfavourable fate was seen in 26 (15.57%) in category I, 45 (71.43%) category II and only 6 (8.11%) in category III. The proportion of unfavourable fate in retreatment cases was significantly more than new cases (χ^2= 8.5, p <0.05).

Past history of TB i.e. defaulted; failure, relapse and other type TB cases were also significantly associated with increased risk of death, p 0.01. History of contact was highly significantly associated with increased risk of death, p<0.01.High proportion of cases visiting to government institute was at more increased risk of becoming unfavourable fate. This may be due to more number and more severe cases visited at government institute than private, p<0.001 Other variables such as type of lesion, type of patient and delay in initiation of treatment were not significant for death. Their p values were >0.05.Thus, in Univariate analysis, higher unfavourable rates were associated with past history of TB and first action at government institute

Table No. 5. Prediction Model of Risk factors for unfavourable fate.

Risk factors	B	S.E.	Wald	Sig.	Exp(B)	95% Confidence Interval for Exp(B)	
						Upper	Lower
Age above 35 years	1.734	0.39	19.757	0.00	5.664	2.636	12.166
Married	1.419	0.653	4.724	0.03	4.134	1.15	14.869
Illiteracy	1.03	0.361	8.15	0.004	2.802	1.381	5.686
Past h/o TB	-0.963	0.389	6.127	0.013	0.382	0.178	0.818
First action at government institute	1.126	0.479	5.52	0.019	3.082	1.205	7.881
Constant	-3.26	0.58	31.594	0	0.038	-	-

In forward stepwise logistic regression, criteria for variables was set at p<0.1for inclusion and >0.5 for removal. Significance level was at p<0.05. All the variables from univariate analysis were put for step wise selection and removal process in the logistic regression analysis. The final model was obtained at 5th step. The set of

variables which determines the prediction model for increased risk of unfavorable cases were age above 35 years, married, illiteracy, past history of TB and first actions at government institutes.

DISCUSSION

The present study revealed that in univariate analysis, higher death rates were associated with above 35 years of age, male and illiterate TB cases, smoking, drinking, kaccha house, unsatisfactory premises, past history of TB and first action at government institute. Sadacharam K et al revealed that mortality was significantly higher among patients aged > 40 years than among patients < 40 years (22% vs 8%). [6] Similarly, a higher proportion of mortality was significantly associated with male sex, unemployment, smoking, drinking, first action at government center and having body weight < 40 kg. Vasantha T et al had shown higher death rates were independently associated with patient's age (45 years), previous history of treatment and alcoholism. [7] Duarte EC et al reported that the factors associated with a higher risk of death included gender (males: odds ratio (OR) 1.4; 95% confidence interval (CI) 1.33 to 1.47), age (<5 years of age: OR 1.90; 95% CI 1.51 to 2.38; 30–59 years: OR 2.78; 95% CI 2.61 to 2.97; over 60 years: OR 10.92; 95% CI 10.09 to 11.81), alcoholism (OR 1.49; 95% CI 1.36 to 1.65. Protective variables included education (highest level: OR 0.67; 95% CI 0.63 to 0.70). [8] Santha T et al reported that in univariate analysis, higher death rates were associated with history of treatment and delayed care-seeking behavior. Age, sex, literacy, alcoholism and employment status were not predictive of death. [7]

The present study had shown the prediction model for increased risk of unfavorable cases included the following variables; age above 35 years, married, illiteracy, past history of TB and first actions at government institutes were independently associated with higher death rates. Sadacharam K et al reported that in multivariate analysis, a higher mortality rate was independently associated with age, sex, occupation and treatment outcome. [6] Bao QS et al reported that reported that in multivariate analysis, treatment success was found to be associated with young age, lack of cavitations and compliance with treatment. [9] TuulaVasankari T et al reported significant independent risk factors for death in multinomial logistic regression model were male sex and age. [10] Santha T et al reported that in multivariate analysis, higher death rates were independently associated previous history of treatment (AOR 3.3, 95%CI 1.5–7.0). [7] Vijay S et al reported in the logistic regression analysis, factors independently associated with default were alcoholism, illiteracy, having other commitments during treatment, inadequate knowledge of TB, poor patient provider interaction, lack of support from health staff, having instances of missed doses, side effects to anti TB drugs and dissatisfaction with services provided. [11]

CONCLUSION

This study may add the knowledge on TB, time trend for mortality and natural dynamic of TB disease. The risk factors derived by logistic regression may be applied to identify lacunae/ obstacles due to which patients land up in unfavourable fate. More inputs should be provided for motivating the cases and their families regarding to strengthen their hold on DOTS chemotherapy and to prevent morbidity and mortality.

Limitations of the study: The time of initiation of DOTS was different for all cases. Since it was not possible to get interview on exact date after two years of DOTS, this lacuna remained while

conducting the study. Cases with TB disease were more than two years ago and also those died, cause of death ascertained through family members by verbal autopsy. These recall bias exits which could not be removed. The non-traceable cases were 14.85%.

ACKNOWLEDGEMENT

The authors would like to acknowledge WHO Consultant for Tuberculosis for immense help and technical support, City TB Officer (CTO) for providing secondary data on TB register and DOT providers for their help to locate tuberculosis cases.

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How to cite this article: Dandekar RH, Dixit JV. Risk factors for unfavourable fate cases after two years of Directly Observed Treatment Short Course Chemotherapy (DOTS). Int J Health Sci Res. 2014; 4(5):14-20.

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