Original article

Risk factors for unsuccessful tuberculosis treatment outcome (failure, default and death) in public health institutions, Eastern Ethiopia

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Abstract

Background: Unsuccessful TB treatment outcome is a serious public health problem. Therefore, this study aims at identifying risk factors for unsuccessful TB treatment outcome in eastern Ethiopia.

Methods: Intuitional based case-referent study was employed on patients' records in six TB clinics that had been providing DOTS in eastern Hararge Zone, Dire Dawa City Administration, and Harari Regional State. The cases were the records of TB patients registered as defaulter, dead and/or treatment failure. The controls were the patients who were cured or who completed the treatment. Multivariate logistic regression model was used to derive adjusted odds ratios (OR) at 95% CI to examine relationship between the unsuccessful TB treatment outcome and patients' characteristics.

Results: A total of 976 sample size (330 cases and 646 controls) were included. Of the cases 212 (64.2%) were dead, 100 (30.3%) defaulters and 18 (5.5%) were treatment failure. In this study, the factors independently associated with the unsuccessful TB treatment outcome include: lack of contact person(OR=1.37; 95% CI 1.14-2.9, P, .024), smear negative treatment category (OR=1.8; 95% CI 1.3-5.5,P, .028), smear positive sputum test at 2nd month after initiation of treatment (OR=14; 95% CI 5.5-36, P,0.001) and HIV positive status(OR=2.5; 95% CI 1.34-5.7, P, 0.01).

Conclusion: Many of the unsuccessful TB treatment outcomes wee because of death. TB patients who do not have contact person, smear negative treatment category, smear positive at second month after initiation of treatment and HIV positive status were significantly associated with unsuccessful treatment outcome. Targeted management of TB patients who are smear positive after second month of treatment initiation, HIV positive and do not have contact person should be considered through the entire TB treatment period. [*Ethiop. J. Health Dev.* 2014;28(1):17-21]

Background

Tuberculosis (TB) is the major cause of illness and death in sub-Saharan African countries and Ethiopia ranks third in TB case incidence rate in the region. The burden is intensified by the spread of HIV in the country (1, 2).

In Ethiopia, although a free TB diagnosis and treatment is integrated into the general health services, DOTS geographical coverage is above 95% and has been provided by more than 1,448 state-owned and 230 private health facilities. TB has remained a major health problem. The cure rate (67%) has remained well below the WHO recommendation (85%) (3). In a study done in Southern Ethiopia, 20% of TB patients still face unsuccessful treatment outcome. A retrospective study in rural hospitals in Ethiopia found out that the rate of defaulting from treatment was 11.4%. Another study from northern Ethiopia revealed that among unsuccessful treatment outcome 18.3% were defaulters, 10.1% dead and 0.2% were treatment failure (4-6).

In effort to reach the global target of 85% treatment success, it is compelling to identify, describe, and deal with factors determining unsuccessful TB treatment outcome. Several reasons and risk factors for unsuccessful TB treatment outcomes have been reported from different countries (4, 5, 7, 8). However, not clear which factors are main contributors to unsuccessful

treatment outcome of TB patients in the eastern part of Ethiopia. Therefore, this study, by focusing on the health institutions providing DOTS, was aimed to filling this gap.

Generally, unsuccessful treatment outcome is believed to be the main reason for difficulties in controlling a disease that is far from new. For these reasons, determination of the factors that predicts the unsuccessful treatment outcome helps to design the possible future of TB treatment and control in the community. Therefore, this study is aimed at describing the main forms of unsuccessful TB treatment outcome and associated factors among health institutions providing DOTS in East Hararge Zone of Oromia Region, Dire Dawa Administration and Harari Regional State, Eastern Ethiopia.

Methods

Settings and Study Design:

Intuitional based case referent study was employed on patients' records in six randomly selected TB clinics that had been providing DOTS in East Hararge Zone of Oromia Region, Dire Dawa Administration and Harari regional State. The cases were those registered as defaulters, death, or treatment failures on the TB registration log books. The controls were TB patients, who were recorded closest to the case before or after and

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declared as cured or treatment complete. For each case, two controls were selected. Data was collected from September 1st to October 30, 2012.

Sample Size and Sampling Procedures:
The sample size was calculated based on the assumption of defaulter to treatment as one of the important risk factors for unsuccessful treatment outcome, 5% level of significance and 80% power. In an earlier study, we found out that the proportion of successful treatment outcome among re-treatment after default was 46% while 55% of patient returns after default result in unsuccessful treatment outcome (7). Based on the above assumption the final sample size was 330 cases and 660 controls with 95% certainty that return after default is a statistically significant risk factor for unsuccessful TB treatment. TB patients' records from September 2007 to   August 30, 2012 were reviewed.   The total sample size was proportionally allocated to each institution based on the number of patients who started TB treatment in the institution in the last five years, before the data collection. The total sample size allocated for each institution was also distributed to each year proportional to the number of TB patients started treatment in that year (2007-2012).   All the list of defaulters, dead or treatment failure patients was reviewed until the sample size was fulfilled. To improve the comparison, for one case two controls, who started treatment closest to the case in the same institution, were included.

Data Collection:
The data were collected using a check list prepared from TB registration logbook which was developed by the Ministry of Health. The check lists were filled out by health workers working in the TB clinics. To ensure the quality of data, the check list was pre-tested in one hospital and one health centre, which were not included in the study. Training was given for data collectors and the data collection process was supervised by the investigators. Every check list was checked for its completeness during the data collection.

Data Analysis and Processing:
The data were coded and entered into Epi-data and transferred to SPSS Version 17.0.for analysis. Descriptive statistics was carried out to explore the background characteristics. A stepwise logistic regression model was used to examine the relationship between the outcome variable and the selected factors. The variables recorded on the TB registration logbook were included in the logistic regression to determine the predictors of unsuccessful TB treatment outcome. Odds ratio (OR) with 95% CI was calculated as a measure of association. P-values equal to or below 0.05 were considered statistically significant.

Ethical Considerations:
The study protocol was approved by the Institutional Research Ethics Review Committee of the College of Health and Medical Sciences of Haramaya University.

In order to protect the confidentiality of the information, names or Identification numbers were not included in data extraction check list.

Results
Socio-demographic Characteristics:
Records of 330 (33.8%) cases and 646 (66.2%) controls were analyzed. Fourteen controls were excluded during data entry because most part of basic information of patients had not been filled out. Among the total sample included in analysis, many were female (63.6% cases vs 57.9% controls), who were between 20 to 34 years of age (59.3% case vs 61% controls) with a mean age of 32 (34.9 years among cases vs 30.9 years among controls). Moreover, 651 (66.7%) (57.3% case vs 71.5% control) had contact person. From patient included in the analysis majority had HIV test (68.4% of cases and 72.4% controls). Among the HIV tested study participants, 35.9% of the cases and 24.2% of the controls were HIV positive (P< 0.002) (Table 1).

TB Treatment Related Characteristics:
Among the cases (n=330), many were recorded as death (64.2%), some as defaulters (30.3%), and very few as treatment failures (5.5%). Among the total patients, most of them 802 (82.2%) were pulmonary Tuberculosis (PTB) (80.9% of cases vs 81.8% of controls) of whom 47.3% of the cases and 32% of the controls (P<0.001) were smear negative PTB. Of the smear positives, 13 (4.2%) were smear positive again at the second month after starting treatment, with significant difference between cases and controls (35.4% of the cases and 4% of the controls) (P<0.001). Most of the cases (85.5%) and the controls (88.1%) were in new treatment category. About 10.6% of the cases and 9% of the controls   had history of previous unsuccessful treatment outcome, and this was because of relapse (7.3% of the cases and 5.4% of the controls), default (1.8% of the cases and 3.3% of the controls), and treatment failure (1.5% of the cases and 0.3% of the controls) (Table 1).

Factors Associated with Unsuccessful TB Treatment Outcome:
To evaluate factors associated with unsuccessful TB treatment outcome gender, age, presence of contact person, TB diagnosis category, treatment category (new vs previously unsuccessful), HIV status and sputum result at 2nd month after initiation of treatment were entered into multiple logistic regression analysis. Lack of contact person at a time of treatment interruption (AOR 1.37; 95% CI 1.14-2.91, P=0.024) and smear negative diagnosis (OR 1.83; 95% CI 1.3-5.51, =0.028) were associated with unsuccessful TB treatment outcome. HIV positive status (OR 2.3; 95% CI 1.34-5.73, P= 0.002) and positive sputum test result at second month after initiation of treatment (OR 14.2; 95% CI 5.52-36.46, P< 0.001) were also independently associated with the unsuccessful treatment outcome (Table 2).

Table 1: **Characteristics of patients started DOTS in selected health institutions in eastern Ethiopia from September 2007 to August 30, 2012**

Variables	Frequency (%)		P-Value
	Case (Unsuccessful)	Control (Successful)	
Sex			
Male	210 (63.6)	374 (57.9)	0.083
Female	120 (34.4)	272 (42.1)	
Age in Year			
9 and below	18 (5)	44 (6.8)	
10-19	26 (7.9)	82 (12.7)	0.019
20-29	94 (28.6)	199 (30.9)	
30-34	101 (30.7)	194 (30.1)	
45 and above	90 (27.4)	125 (19.4)	
Have contact person			
Yes	189 (57.3)	462 (71.5)	0.001
No	141 (42.7)	184 (28.5)	
HIV test offered			
Yes	206 (68.4)	435 (72.4)	0.21
No	95 (31.6)	166 (27.6)	
HIV test result			
Sero positive	74 (35.9)	105 (24.2)	0.002
Sero negative	132 (64.1)	328 (75.8)	
Treatment category			
New	282 (85.5)	569 (88.1)	
Relapse	24 (7.3)	35 (5.4)	
Treatment Failure	5 (1.5)	2 (0.3)	0.087
Defaulters	6 (1.8)	21 (3.3)	
Transfer in	13 (3.9)	19 (2.9)	
Diagnosis category			
Pulmonary positive (P.Pos)	112 (33.6)	335 (49.8)	0.001
Pulmonary negative (P/Neg)	150 (47.3)	205 (32)	
Extra pulmonary (EP)	68 (19.1)	106 (8.1)	
Sputum AFB result at 2nd month after initiation of treatment			
Positive	17 (35.4)	13 (4)	0.001
Negative	31 (64.6)	314 (96)	

Table 2: **Factors associated with unsuccessful TB treatment outcome n selected health institution in eastern Ethiopia, 2013**

Variables	Unsuccessful treatment outcome		P-Value
	COR	AOR	
Sex			
Male	1.3 (0.97-1.7)	1.05 (0.53-2.20)	0.88
Female	1.00	Reference	
Age			
15 and less	0.53 (0.32-0.89)	0.8 (0.14-3.90)	0.7
16-44	0.66 (0.48-0.90)	1.3 (0.23-7.60	0.18
45 and above	1.00	Reference	
Have contact person			
Yes	1.87 (1.42-2.47)	1.37 (1.14-2.91)	0.024
No	1.00	Reference	
Sputum smear result at the beginning of treatment			
Smear negative	2.2 (1.6-2.95)	1.83 (1.3-5.51)	0.028
Extra pulmonary (EPT)	1.4 (0.96-2.02)	1.54 (0.7-4.39)	0.155
Smear positive	1.00	Reference	
Treatment category			
Previously unsuccessful	1.3 (0.9-1.85)	0.94 (0.34-2.60)	0.09
New	1.00	Reference	
HIV Status			
Positive	1.81 (1.32-2.52)	w.53 (1.34-5.73)	0.01
Negative	1.00	Reference	
Sputum AFB result at 2nd month after initiation of treatment			
Positive	13.25 (5.90-29.80)	14.23 (5.52-36.46)	0.001
Negative	1.00	Reference	

Discussion
This study has attempted to identify the risk factors of unsuccessful TB treatment outcomes in eastern Ethiopia. It reviewed 976 records (330 cases and 646 controls) recorded from 1st September, 2007 to 30th October, 2012 in six TB clinics of public health institutions in eastern Ethiopia. Out of the total reviewed patients' record a significant proportion of unsuccessful treatment outcome were pulmonary negative (47.3% of cases and 32% of controls, P<0.001). This study also demonstrated positive HIV status, positive sputum test result at second month after initiation of treatment, smear negative TB diagnosis category and lack of contact person were the factors significantly associated with unsuccessful treatment outcome after adjust for other variables.

Among the total patients with unsuccessful treatment outcome (n=330) 64.2% were recorded dead. This is similar to a study done on adults in Taipei, Taiwan, which reported death as the main cause of unsuccessful treatment outcome of Tuberculosis patients (8); but it is different from a research which identified defaulter as a major cause in northern Ethiopia (4). The difference might be related with starting of using strategies such as health extension workers to increase public awareness on the importance of effective completion of TB treatment; use of phone of contact person to ascertain reason for lost follow up than before are being undertaken so that might contribute to the decreasing of defaulter from TB treatment .

The main concern about TB/HIV co-infection is that , different study result from different part of the world showed the success of TB treatment outcome are significantly different between HIV positive and HIV negative TB patients. The prevalence of HIV was 35.9% among patients with unsuccessful treatment outcome, but it was 24.2% among the patients who successfully completed the treatment. This showed the risk of unsuccessful TB treatment outcome is significantly high among HIV positive TB patients compared to HIV negative (OR= 2.33 (1.34-5.73, P<0.01)). It is comparable with many studies that have found TB/HIV co-infections are associated with poor treatment outcome (9-13). One can understand that HIV is continued to be double challenge both in increasing the risk of developing TB and poor outcome of the treatment.

Sputum test positive for AFB result at second month after initiation of treatment was significantly higher among the unsuccessful treatment outcomes compared to the successful treatment outcomes (OR= 14.23(5.52-36.46)). A study from southern Ethiopia showed that TB patients' sputum smears remained positive at second month after initiation of treatment had significantly high risk of unsuccessful treatment outcome. This result is also in line with a study finding from Yunnan, China which showed positive second month smear test result is one of the risk factors for unsuccessful treatment outcome (7, 14). Though no drug resistance survey has been conducted in the area, pulmonary positive TB patients remained positive after second months of treatment initiation may not react well to treatment due to drug resistant Mycobacterium tuberculosis which is one of the risk factors for non-cure.

Our study showed that sputum smear negative pulmonary TB diagnosis category was a factor that predicted unsuccessful TB treatment outcome (OR 1.83, 95% CI 1.3-5.51)). The finding is in line with previous studies from Ethiopia and other countries (4, 8). This might because of probability of miss diagnosis of the patients which resulted with poor treatment response. This study also depicts lack of contact person was the risk factor associated with unsuccessful treatment outcome (OR=1.37(1.14-2.91, p<0.024)).

There are some limitations to this study. First, the retrospective nature of the study is a methodological limitation. Second, we used only routine program data. The Ethiopian health institutions' TB log book might not be an adequate checklist to identify the full history of TB patients. Thus, it is possible that there might be other associated factors left to be examined. The analysis can only provide evidence of statistical association between those items and unsuccessful treatment outcome and cannot show cause-effect relationships. Despite these limitations, the study findings are useful to inform policy makers and programmers that aim to improve the management of TB patients in Ethiopia and other similar settings.

Conclusion and Recommendations:
In summary, this study provides useful insights on factors associated with unsuccessful treatment outcomes. Death was the major unsuccessful treatment outcome of tuberculosis patients in the study area. AFB smear positive on second month after initiation of treatment was significantly associated with unsuccessful treatment outcome. Our results also confirmed previous findings that assert that TB/HIV co-infection is a factor associated with increased risk of unsuccessful treatment outcome. Lack of contact person and smear negative pulmonary TB diagnosis category were also the factors significantly associated with high unsuccessful treatment outcome. TB patients those who are HIV positive and don't have contact person need strict follow up throughout DOTs period. Moreover, even though DOTS is only for intensive care those who became smear positive after second month of TB treatment initiation should be considered for daily basis follow up. Prospective study is needed in the study area to identify main cause of the unsuccessful TB treatment outcome.

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