

Profile and treatment outcomes of patients with tuberculosis in Northeastern Ethiopia: a cross sectional study.

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Abstract:

Background: Data on the epidemiology of tuberculosis and its treatment outcomes were incomplete in the study area and this study was done to fill this gap.

Methods: Institution based cross sectional study was conducted from January 2011 to December 2014. A total of 949 TB patients who were on treatment in North Eastern Ethiopia, Eastern Amhara region were included. Data was analyzed using SPSS version 20. Frequency, percentages and means were used to present data. To assess the associations of treatment outcomes with sex, age, type of TB and human immunodeficiency virus (HIV), logistic regression was used.

Results: The proportion of smear positive and negative pulmonary TB, and extra pulmonary TB were 187/949 (19.7%), 322/949 (33.9%) and 440/949 (46.4%), respectively. Treatment success rate was 853/949 (89.9%). Smear positive pulmonary TB and TB/HIV co-infections were significantly associated with unsuccessful treatment outcome, $P \leq 0.002$.

Conclusion: Extra pulmonary TB was the most prevalent types of TB followed by smear negative pulmonary TB. Treatment success rate was above the WHO target of 85%. The causes for the high proportion of smear negative PTB and EPTB should be further investigated. Special emphasis should be put on smear positive PTB patients and TB/HIV co-infected patients to decrease unsuccessful treatment outcome and TB transmissions.

Keywords: Tuberculosis, types of tuberculosis, treatment outcomes, Ethiopia.

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Background

Tuberculosis (TB) is a disease of centuries. It killed more persons than any other infectious diseases¹. Tuberculosis is a disease of poverty and mainly affects poor countries. A person with TB loses, on average, 20-30% of annual household income due to illness².

Acid fast bacilli (AFB) microscopy with spot-morning-spot sputum sample collection strategy was the recom-

mended technique for the diagnosis and follow-up of pulmonary TB (PTB) patients in the Directly Observed Treatment short course (DOTS) program³⁻⁵. Effective treatment of TB started in 1946, with the introduction of streptomycin (SM). The main problem with current chemotherapy is too long duration of treatment regimen thus allowing opportunities for interruptions in drug taking that may lead to the emergence of drug resistance⁶.

Globally, the rate of treatment success among new smear-positive PTB who were treated in the 2012 cohort was 86%. Treatment success rate was higher among smear positive PTB than smear negative PTB⁷. In Ethiopia in the same year, TB treatment success rate among new TB cases was 91%⁵. However; it is unknown among retreated cases⁵.

There was no data about TB treatment outcome in the study area in particular. In addition, aggregate national

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data might not reflect the real TB profile and treatment outcomes due to subtle socioeconomic, geographic and methodological variations. Thus, studies like this might show the appropriate proportion of mean treatment outcome and types of TB in the specific area. Thus, this study was done to determine the profile and treatment outcome of TB patients in Amhara National Regional State (ANRS); Kobo and Raya Kobo Woredas of Ethiopia.

Materials and methods

Study setting, period and population

Institution based cross-sectional study was conducted on patients diagnosed and treated over the period of January 2011 to December 2014 in Kobo, Robit and Gobiye health centers. These health centers found in eastern Amhara region in north wollo zone, 552km away from Addis Ababa. The woredas are part of a mid-altitude area which lies between the Ethiopian Highlands to the west and the Afar depression to the east. Currently, there are 8 additional health centers in the studied area that provide TB diagnosis and treatment. However, these health centers were newly opened and had incomplete registration system to be included in the study.

Tuberculosis diagnosis and treatment strategy

The pulmonary TB diagnosis and treatment was based on the stop TB strategy. That is, sputum samples were collected using spot-morning-spot strategy and three slides were prepared, one from each sample. Slides were processed and examined using the standard Ziehl-Neelsen (ZN) AFB staining technique⁸.

Extra pulmonary TB was diagnosed at nearby government and private health institutions primarily based on clinical data with limited service of imaging and pathological examinations. Diagnosis of TB in children was based on clinical and X-ray findings.

For those patients diagnosed with active TB, the standard TB treatment regimen; 2(RHZE)/4 (RH) and 2S (HRZE)/1(HRZE)/5(HR) E were administered for new and previously treated TB patients respectively⁹.

Operational definitions

Health Center: A primary health care unit that serves a population of 15,000-25,000 and is comprised of specialized clinics like TB, antiretroviral treatment (ART), maternal and child health clinics.

Inclusion and exclusion criteria

All TB patients with complete demographic and clinical data were included in the study. Whereas, patients with unknown types of TB and treatment outcomes, including transferred out were excluded.

Data collection and tools

Demographic and clinical data such as age, sex, type of TB, TB treatment outcome, status of human immunodeficiency virus (HIV) infection, co-trimoxazole prophylaxis (CPT) and antiretroviral treatment (ART) status were retrieved from TB registry using data extraction sheets.

Data analysis

Collected data was entered, cleared, and analyzed using SPSS statistical software package (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.). Frequency, percentage, mean and standard deviation (SD) were used to present data. To assess the associations of treatment outcome with sex, age, type of TB and HIV status; stepwise logistic regression model was used. Variables with a p-value of ≤ 0.2 PubMed in bi variate analysis were included in the multivariate analysis. Associations were determined using odds ratio and 95% confidence interval. A p-value of < 0.05 was considered to indicate statistical significance.

Ethics statements

This study was approved by Amhara Regional Health Bureau Institutional Ethical Review Board (IRB) to utilize the data. No patient details that may link to the patient identity were used and the confidentiality was maintained.

Results

Demographic epidemiology of tuberculosis

Among the total of 990 TB patients registered on TB notification books, 30 (3%) were transferred out and 11 (1.1%) were with unknown treatment outcomes. We excluded these categories of patients. Thus, data from a total of 949 TB patients were included for analysis. Of the total included, 528/949 (55.4%) were males. Mean age of participants were 32.8 years with SD of 16.3. Moreover, high proportions of TB patients; 285/949 (30%) and 212/949 (22.3%) were in the age groups of 25-34 and 15-24 years, respectively [Table 1].

Table 1: Distribution of demographic characteristics and HIV status among tuberculosis patients in Kobo and Raya Kobo Woredas-Ethiopia, 2015.

Variables	Type of Tuberculosis				Total N (%)
	PTB ⁺ N (%)	PTB ⁻ N (%)	EPTB N (%)		
Sex	Female	91 (48.6)	133 (41.3)	197 (44.7)	421 (44.5)
	Male	96 (51.4)	189 (58.7)	243 (55.3)	528 (55.5)
Age	<=14	5 (2.7)	29 (9)	61 (13.9)	95 (10)
	15-24	51 (27.3)	66 (20.5)	95 (21.6)	212 (22.3)
	25-34	70 (37.4)	94 (29.2)	121 (27.5)	285 (30)
	35-44	25 (13.4)	43 (13.3)	53 (12)	121 (12.7)
	45-54	18 (9.6)	44 (13.6)	47 (10.7)	109 (11.5)
	55-64	11 (5.9)	21 (6.5)	38 (8.6)	70 (7.4)
	>=65	7 (3.7)	25 (7.7)	25 (5.7)	57 (6)
	HIV Status	Unknown	6 (3.2)	6 (1.8)	6 (1.4)
	Positive	65 (34.8)	87 (27)	75 (17)	227 (24)
	Negative	116 (62)	229 (71.1)	35 9(81.6)	704 (74.2)
Total		187 (19.7)	322 (33.9)	440 (46.4)	949 (100)

Profile of tuberculosis

The proportion of smear positive PTB, smear negative PTB and EPTB were 187/949 (19.7%), 322/949 (33.9%) and 440/949 (46.4%), respectively [Table 1]. There was no significant difference on the types of TB with regard to sex and age of participants. The proportion of TB/HIV co-infection was 227/949 (24%). Moreover, TB/HIV co-infection was twice higher among smear positive PTB than EPTB [Table 1].

Tuberculosis treatment outcomes

The overall unsuccessful treatment outcome was 96/949 (10.1%) wherein failed, died and lost to follow up shared at 21/949 (2.2%), 47/949 (5%) and 28/949 (2.9%) respectively. It is found that the proportion of unsuccessful TB treatment outcome was higher among male and older age patients than their counterparts with no statistical significance. On the other hand, the proportion of cured was at 132/949 (13.9%) and treatment completed at 721/949 (76%) [Table 2].

Table 2: Distribution of tuberculosis treatment outcomes by demographic and profile of TB patients, Kobo and Raya Kobo Woredas-Ethiopia, 2015.

Variables		Tuberculosis Treatment out come						Total N	
		Successful			Unsuccessful				
		Cured N (%)	Completed N (%)	Sub total N (%)	Failed N (%)	Died N (%)	LTF N (%)		Sub total N (%)
Sex	Female	63 (47.7)	316 (43.8)	379 (44.4)	12 (57.1)	19 (40.2)	11(39.3)	42 (43.7)	421
	Male	69 (52.3)	405 (56.2)	474 (55.6)	9 (42.9)	28 (59.6)	17 (60.7)	54 (56.3)	528
Age	0-14	5(3.7)	86 (11.9)	91 (10.7)	2 (9.5)	0 (0.0)	2 (7.1)	4 (4.2)	95
	15-24	36 (27.3)	155 (21.5)	191 (22.4)	7 (33.3)	9 (19.1)	5 (17.9)	21 (21.9)	212
	25-34	54 (40.9)	206 (28.6)	260 (30.5)	7 (33.3)	9 (19.1)	9 (32.1)	25 (26.0)	285
	35-44	16 (12.2)	91 (12.6)	107 (12.5)	1 (4.8)	9 (19.1)	4 (14.3)	14 (14.6)	121
	45-54	10 (7.6)	86 (11.9)	96 (11.3)	2 (9.5)	8 (17.0)	3 (10.7)	13 (13.5)	109
	55-64	6 (4.5)	52 (7.2)	58 (6.8)	1 (4.8)	7 (14.9)	4 (14.3)	12 (12.5)	70
	≥65	5 (3.7)	45 (6.2)	50 (5.9)	1 (4.8)	5 (10.6)	1 (3.6)	7 (7.3)	57
Type of TB	PTB ⁺	127 (96.2)	25 (3.5)	152 (17.8)	14 (66.7)	14 (29.8)	7 (25)	35 (36.5)	187
	PTB ⁻	0 (0.0)	296 (41.1)	296 (34.7)	3 (14.3)	14 (29.8)	9 (32.1)	26 (27.1)	322
	Extra PTB	5 (3.8)	400 (55.5)	405 (47.5)	4 (19.0)	19 (40.2)	12 (42.9)	35 (36.5)	440
HIV status	Unknown	5 (3.8)	10 (1.4)	15 (1.8)	0 (0.0)	0 (0.0)	3 (10.7)	3 (3.1)	18
	Positive	40 (30.3)	148 (20.5)	188 (22.0)	7 (33.3)	24 (51.1)	8 (28.6)	39 (40.6)	227
	Negative	87 (65.9)	563 (78.1)	650 (76.2)	14 (66.7)	23 (48.9)	17 (60.7)	54 (56.3)	704
Total		132 (100)	721(100)	853 (100)	21 (100)	47 (100)	28 (100)	96 (100)	949 (100)

Furthermore, significant differences were observed on treatment outcome between smear positive PTB and EPTB, and between HIV positive and HIV negative TB patients [Table 3].

Table 3: Association of unsuccessful treatment outcomes with possible predictors among tuberculosis patients, Kobo and Raya Kobo Woreda-Ethiopia, 2015.

Variables	TB treatment outcome			Over all P-value of binary regression	AOR (95% CI), P-value
	Unsuccessful N (%)	Success full N (%)	Total (N)		
Sex:				0.89	
Male	54 (56.3)	474 (55.6)	528		-
Female	42 (43.7)	379 (44.4)	421		
Age:				0.17	
0-14	4 (4.2)	91(10.7)	95		0.3(0.08-1), 0.06
15-24	21 (21.8)	191 (22.4)	212		0.64(0.2-1.6), 0.35
25-34	25 (26.0)	260 (30.5)	285		0.4(0.16-1.07), 0.07
35-44	14 (14.6)	107 (12.5)	121		0.65(0.24-1.7), 0.4
45-54	13 (13.5)	96 (11.3)	109		0.79(0.3-2.1), 0.66
55-64	12 (12.5)	58 (6.8)	70		1.3(0.5-3.8), 0.5
≥65	7 (7.3)	50 (5.9)	57		1
Types of TB:				0.0001	
PTB+	35 (36.5)	152 (17.8)	187		2.3(1.3-3.8), 0.02
PTB-	26 (27.1)	296 (34.7)	322		0.88(0.5-1.5), 0.6
EPTB	35 (36.4)	405 (47.5)	440		1
HIV Status:				0.0001	
Unknown	3 (3.1)	15 (1.8)	18		2.6(0.7-9.6), 0.15
Positive	39 (40.6)	188 (22.0)	227		2.6(1.6-4.27), 0.001
Negative	54 (56.3)	650 (76.2)	704		1
Total	96(10.1)	853 (89.9)	949		

Discussion

This study revealed high proportion of TB among males than females. This agreed with different findings reported in Ethiopia and abroad^{5,10-13}. The possible reason might be related with, lower rates of notification of TB among women than men due to low health seeking behavior, lack of financial control and stigma associated with being TB positive². Majority, at 22.3% and 30% of TB patients were in the age groups of 15-24 and 25-34 years respectively. This report is also in line with other literatures^{5,10,14-15} which indicated that, TB mainly affects the reproductive

segment of the population. This might be due to high HIV prevalence in these age groups (personal opinion).

The TB profile data showed that high proportions of TB patients were EPTB and smear negative PTB which is comparable with other Ethiopian TB profile data¹⁶. However, it is in contrary with reports from outside Ethiopia^{5,14,17-18}. Currently, two justifications seems plausible: the role of false positive²⁰/over prescription/ and the zoonotic transmission, social and host-pathogen genomic factors²¹. These two justifications are presented as follows;

The first argument discussed that, most of EPTB and smear negative PTB cases were diagnosed and transferred in from private health facilities. However, these facilities might not have well organized facilities and expertise to diagnose EPTB and smear negative PTB cases. This is in line with studies by Iwnetu et al. and Ehlers et al. According to these studies, up to 15% of all EPTB and 97.3% smear negative PTB cases were diagnosed wrongly¹⁹⁻²⁰. Furthermore, clinicians might abused the low sensitivity of ZN and low specificity of pathological tests and might rushed to diagnose presumptive TB cases as confirmed smear negative PTB/EPTB (expert opinion)

The other justification goes in line with Berg et al, study justified that regular and direct contact with live animals, was a significant risk factor for EPTB²¹. These factors also seem likely, because, people in the study area are known live stock keepers and due to their local tradition, most of their domestic animals shared human shelter. Moreover, these people regularly use raw meat and milk. Moreover, the high smear negative PTB might be due to difference in the immunological and nutritional status of Ethiopian with other counties (unpublished report). However, to identify the real cause of such high prevalence report in Ethiopia, it needs further comparative ecological and cohort study.

In the present study, the proportion of TB/HIV co-infection was at 227/949 (24%), much higher than WHO report of the year 2015²². Moreover, TB/HIV co-infection was twice higher among smears positive PTB than EPTB which is in contrary with a literature²³. This can be explained by tailoring to Ethiopian situation. If the reports of Iwnetu et al. and Ehlers et al., mentioned above, considered as a possible cause for high rate of EPTB and smear negative PTB in Ethiopia, this would also dilute the TB/HIV co-infection rate among EPTB and smear negative PTB patients.

The odd of having unsuccessful treatment outcome was 2.3 times higher among smear positive PTB than EPTB patients (AOR: 2.3; 95% CI: 1.3-3.8; P: 0.02). This might be due to higher HIV prevalence, (34.8%) among smear positive PTB than smear negative PTB (27%) and EPTB (17%) [Table 1]. Similar finding was reported from Addis Ababa²⁴.

The odds of having unsuccessful TB treatment outcome was 2.6 times higher among TB/HIV co-infected than HIV negative TB patients (AOR: 2.6; 95% CI: 1.6-4.27; $p < 0.0001$) (Table 3). This might be due to low level of immunity and drug mal-absorption²⁵. This finding was in line with a study from Addis Ababa, Eastern Ethiopia, Benin and Malawi^{15,24,26,27}. Furthermore, the proportion of unsuccessful treatment outcome was higher among TB/HIV co-infected people with no history of CPT and ART than those on CPT and ART [data not shown]. Administration of ART is recommended during TB therapy regardless of the CD4 cell count,²⁸ because ART is associated with reduction in mortality and HIV disease progression²⁹⁻³². Moreover, all HIV-infected patients with active TB should receive CPT^{30,22}

Limitation of the study

The recorded data lack detail clinical profile like CD4 count and other comorbidities. On top of this, due to the inherent limitation of the study design, the study couldn't show any cause effect relation between significantly associated variables.

Conclusions and recommendations

The proportion of smear negative PTB and EPTB were higher than smear positive PTB cases. Plus, the overall TB treatment success rate was above the WHO target of >85%. Moreover, smear positive PTB and TB/HIV co-infections were significantly associated with unsuccessful TB treatment outcomes. Thus, we would like to forward the following recommendations; (1) the causes for the high proportion of smear negative PTB and EPTB cases should be further investigated. (2) The ART and CPT coverage must reach 100% to TB/HIV co-infected patients so that their unsuccessful treatment outcome rate would be improved. (3) Especially emphasis should be paid to smear positive PTB patients to decrease unsuccessful treatment outcome and decrease transmissions.

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Competing interests:

We the authors declare that we have no competing interests.

Authors' contributions

DM substantially contributed in the design, statistical analysis, interpretation of data and drafting the manuscript. AD was involved in the data collection and entry, statistical analysis and enriched the manuscript. HM was involved in data collection, entry, and analysis. YZ critically revised the table and whole manuscript for intellectual contents. All the authors read and approved the final manuscript.

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