RESEARCH PAPER

Human immunodeficiency virus as a determinant of tuberculosis treatment outcome in tuberculosis patients treated at Arba Minch General Hospital: a five-year retrospective study

Alemu Chemeda Ifa

Department of Biology, College of Natural Science, Arba Minch University, Arba Minch, Ethiopia

Abstract

Introduction: Tuberculosis/human immunodeficiency virus (TB/HIV) co-infection has a mutual and synergistic effect which mostly affects interventions that have been taken on the area. TB/HIV co-infected patients have a worse treatment outcome as compared to HIV-negative patients. There are limited data regarding the impact of HIV on the TB treatment success rate. The aim of this study was to determine the effect of HIV on TB treatment under the implementation of the directly observed treatment strategy.

Material and methods: Five-year retrospective data (from August 2012 to July 2016) of tuberculosis patients (n = 544) registered at the directly observed therapy short-course (DOTS) clinic of Arba Minch General Hospital were reviewed. The association of TB treatment outcome with HIV seropositivity was assessed according to the national tuberculosis control program guideline. Data were entered and analyzed using SPSS version 16. Odds ratios with 95% confidence intervals were used to evaluate the presence and strength of association between TB treatment outcome and HIV status.

Results: Out of the 544 TB patients, 29.2% (159) were HIV co-infected. Overall, the treatment success rate of TB patients with or without HIV was 74.6%. Using cure/completion as a reference, patients with HIV seropositivity had significantly higher odds of default (COR = 1.37; 95% CI: 0.669-2.825), failure (COR = 20.79; 95% CI: 1.065-406.019), death (COR = 6.95; 95% CI: 1.765-27.394) and transfer-out (COR = 2.59; 95% CI: 1.557-4.334).

Conclusions: The rate of treatment success in this study is still lower than the recommended 85% target set by the WHO and Ministry of Health of Ethiopia (97%). In order to further improve the treatment success rate, continuous follow-up with frequent support of patients during the treatment course and strengthening the recording system are strongly recommended.

HIV AIDS Rev 2018; 17, 2: 74-80
DOI: https://doi.org/10.5114/hivar.2018.76376

Key words: treatment success rate, HIV/TB co-infection, Ethiopia.

Address for correspondence: Alemu Chemeda Ifa, Arba Minch University, College of Natural Science, Department of Biology, P.O. Box 21, Arba Minch, Ethiopia, e-mail: chemedashuma1@gmail.com

Article history:
Received: 23.07.2017
Received in revised form: 12.02.2018
Accepted: 25.02.2018
Available online: 21.05.2018

International Journal of HIV-Related Problems
HIV & AIDS Review

Introduction

Tuberculosis (TB) is still a major public health problem in developing countries. It is the second leading cause of death from an infectious disease worldwide, after the human immunodeficiency virus (HIV) [1]. There were an estimated 1.4 million TB deaths in 2015, and an additional 0.4 million deaths resulting from TB disease among people living with HIV. Although the number of TB deaths fell by 22% between 2000 and 2015, TB remained one of the top 10 causes of death worldwide in 2015 [2].

Despite several efforts made to prevent and/or control the disease, many countries have not yet achieved the TB control targets. Rather, it remains a major public health problem leading to mortality in high HIV-burden countries [3, 4]. HIV drives a TB epidemic in many countries, especially in sub-Saharan Africa, where 82% of the world's TB/HIV co-infection exists [2, 5]. The burden of HIV/TB co-infection in the community had a great impact on TB treatment success, which is why TB is a leading cause of mortality and morbidity in developing countries.

Globally, the treatment outcome data show a treatment success rate of 83% for TB, 52% for multidrug-resistant TB (MDR-TB) and 28% for extensively drug-resistant TB (XDR-TB) [2]. According to an Ethiopia Ministry of Health (EMoH) report, in 2015, the TB treatment success rate (TSR) was 92.1%, which is below the target set for the year (97%) [6]. Disparities were observed across regions, with the highest performance being observed in the Southern Nations, Nationalities, and Peoples' (SNNP) Region (97.0%) and the lowest performance was observed in the Gambella Region (66.8%) [7].

To achieve the millennium goal, the synergic activity of HIV/TB is another problem which reduces the TSR. The HIV epidemic is believed to contribute to this inability to reduce TB incidence in Ethiopia. The monitoring of the TB treatment outcome is an essential part of TB disease surveillance to ensure that the disease is successfully eliminated. Despite strong political commitment and implementation of different strategies such as extensive expansion of directly observed therapy short-course (DOTS) services in Ethiopia [8] and the massive involvement of health extension workers (HEWs) in TB prevention and control activities at the grass-root level, and integrated TB/HIV activities in place [7], the key intervention for reducing the burden and mortality of HIV-associated TB was estimated to be low [3, 9].

Since the inception of all the above activities, only a few studies have been conducted in Ethiopia [10, 11]. Furthermore, the impact can vary between different populations and health systems; hence it is important to evaluate the HIV status and treatment outcomes of TB patients in order to perform interventional activities taking into account the specific settings. Therefore, the aim of this study was to assess the impact of HIV status on treatment outcome of TB at Arba Minch General Hospital in the SNNP region of Ethiopia.

Material and methods

Arba Minch is the capital city of the Gamo Gofa zone of the SNNP regional state, in the southern part of Ethiopia. The town is 505 km south of Addis Ababa, the capital city of Ethiopia. Arba Minch General Hospital (AMH) is one of the public health facilities that provide DOTS services for people living in and around Arba Minch town. A five-year retrospective document review of TB patients registered at the DOTS clinic of AMH was conducted to assess the impact of HIV on TB treatment outcome. The study population included all TB cases registered from August 2012 to July 2016 at the AMH DOTS clinic. Patients were diagnosed, registered, treated and referred to other DOTS clinics following the national tuberculosis, leprosy and TB/HIV prevention and control program guideline [7]. Socio-demographic characteristics such as age, sex, residence, and type of tuberculosis infection, status of HIV infection, and outcome of TB treatment were collected from January to March 2017 using a checklist set for this purpose. Patients with incomplete information were excluded. The study was approved by the ethical review committee, College of Medicine and Health Sciences, Arba Minch University. The clinical records of patients were anonymized and de-identified prior to analysis. Consent to collect the information from TB registers was obtained from the AMH administration.

Definitions of treatment outcome

Treatment outcome definitions were used according to the standard definitions of the National Tuberculosis and Leprosy Control Program (NTLCP) [7] and World Health Organization (WHO) guideline [12]. Cured: An initially smear-positive patient who is sputum smear-negative at, or one month prior to, the completion of treatment and on at least one previous occasion (usually at the end of the 2nd or 5th month). Treatment completed: A patient who completed treatment but for whom smear results are not available at the 7th month or one month prior to the completion of treatment. Treatment failure: A patient who remains or becomes again smear-positive at the end of 5 months or later during treatment. Died: A patient who dies for any reason during the course of treatment. Defaulter: A patient who has been on treatment for at least 4 weeks and whose treatment was interrupted for 8 or more consecutive weeks. Transfer out: A patient who started treatment and has been transferred to another reporting unit and for whom the treatment outcome is not known at the time of evaluation of treatment results. Treatment success: The sum of patients who are declared "cured" and those who have "completed" treatment.

Data analysis

Data were entered, cleaned and analyzed using SPSS version 16. Odds ratios with 95% CIs were used to determine the presence and strength of a statistically significant association between HIV status and TB treatment outcome.

Results

Out of 611 TB patients registered between 2012 and 2016 at AMH, 544 patients had complete information (89%). The majority, i.e. 323 (59.4%), of them were male. The mean age was 32.8 years with ± 14.3 years standard deviation (SD). Most of them 385 (70.8%) were HIV-negative TB patients. Many TB cases (335; 61.6%) were pulmonary tuberculosis (PTB) cases. More than 64.7% (352/544) were urban residents (Table 1).

Tuberculosis treatment outcome

Overall, the treatment success rate (TSR) of TB patients with or without HIV during the study period was 406 (74.6%). The remaining 73 (13.4%) were cases of transfer out, 0 (1.8%) were dead, 38 (7%) were defaulters and 3 (0.6%) were cases of treatment failure. Of the HIV-positive patients, 45 (28.3%) were cured, 57 (35.8%) were treatment completed, 7 (4.4%) died, 12 (7.5%) were defaulters, 34 (21.4%) were transferred-out cases, and 3 (1.9) were failures. Of the HIV-negative TB patients, 130 (33.8%) were cured, 187 (48.6%) were treatment completed, 3 (0.8%) died, 26 (6.7%) were defaulters, 39 (10.1%) were cases of transfer-out, while there was no cases of treatment failure. The treatment success rate for TB among HIV-seropositive patients was 64.1% while the treatment success rate for HIV-negative patients was 79%. The treatment success rate among the patients in AMH was generally low, ranging from 60% in 2016 to 79.1% in 2012 with a mean TSR of 74.6%. Failure was reported in two of the five years, 2012 and 2015, while default was reported in all the five years. The rate of cure among the HIV-positive TB cases was 25.7% (45/175) while in HIV-negative cases it was 74.3% (130/175) (Table 2, Fig. 1).

As shown in the above bar graph, the rate of cure was similar in 2013, 2014, and 2015, while it improved in 2016 (Fig. 2).

As shown in the above bar graph, the rate of treatment failure was higher in HIV-seropositive than HIV-negative patients.

Impact of HIV status on tuberculosis treatment outcome

Logistic regression analysis was used by combining the outcome of cured and treatment completed (treatment success) as the reference. HIV-seropositive TB patients had higher odds of death (COR = 6.95; 95% CI: 1.765-27.394) and transfer-out to other health institutions (COR = 2.59; 95% CI: 1.557-4.334). Also HIV-seropositive patients had higher odds of failure (COR = 20.79; 95% CI: 1.065-406.019),

Table 1. The socio-demographic characteristic of tuberculosis patients treated at Arba Minch General Hospital over the five year period

Factor	2012 (*N* = 134)	2013 (*N* = 105)	2014 (*N* = 123)	2015 (*N* = 107)	2016 (*N* = 75)	Total
Age						
< 15	9	2	0	3	1	15 (2.8%)
15-24	13	37	27	29	12	118 (21.7%)
25-34	40	29	44	25	30	168 (30.9%)
35-44	28	31	9	37	11	116 (21.3%)
45-54	23	3	22	6	17	71 (13%)
55-64	16	3	14	5	0	38 (7%)
> 64	5	0	7	2	4	18 (3.3%)
Sex						
Male	99	77	58	54	35	323 (59.4)
Female	35	28	65	53	40	221 (40.6%)
Residence						
Urban	89	67	82	71	43	352 (64.7%)
Rural	45	38	41	36	32	192 (35.3%)
HIV status						
Positive	33	41	29	31	25	159 (29.2%)
Negative	101	64	94	76	50	385 (70.8)
Types of TB						
PTB	98	61	80	56	40	335 (61.6%)
EPTB	36	44	43	51	35	209 (38.4)
Total	134	105	123	107	75	544

PTB – pulmonary tuberculosis, EPTB – extrapulmonary tuberculosis

Table 2. Rate of tuberculosis treatment outcome in patients treated at Arba Minch Hospital between 2012 and 2016

Year	HIV status	No.	Treatment outcome						
			TSR (%)	Cured	Complete	Default	Transfer	Failed	Death
2012	+Ve	33	22 (66.7%)	10 (30.3%)	12 (36.4%)	3 (9%)	5 (15.2%)	1 (3%)	2 (6%)
	–Ve	101	84 (83.2%)	37 (36.6%)	47 (46.5%)	7 (6.9%)	10 (9.9%)	0	0
	Total	134	106 (79.1%)	47 (35%)	59 (44%)	10 (7.5%)	15 (11.2%)	1 (0.7%)	2 (1.5%)
2013	+Ve	41	27 (65.8%)	12 (29.2%)	15 (36.6%)	5 (12.2%)	7 (17%)	0	1 (2.4%)
	–Ve	64	51 (79.7%)	19 (29.7%)	32 (50%)	4 (6.2%)	7 (10.9%)	0	2 (3.1%)
	Total	105	78 (74.3%)	31 (29.5%)	47 (44.8%)	9 (8.6%)	14 (13.3%)	0	3 (2.9%)
2014	+Ve	29	19 (65.5%)	6 (20.7%)	13 (44.8%)	2 (6.9%)	6 (20.7%)	0	2 (6.9%)
	–Ve	94	76 (80.9%)	30 (31.9%)	46 (48.9%)	8 (9.6%)	9 (9.6%)	0	1 (1.0%)
	Total	123	95 (74.8%)	36 (29.3%)	59 (48%)	10 (8.1%)	15 (12.2%)	0	3 (2.4%)
2015	+Ve	31	19 (61.3%)	9 (29%)	10 (32.3%)	0	10 (32.3%)	2 (6.4%)	0
	–Ve	76	63 (83%)	23 (30.3%)	40 (52.6%)	4 (1.3%)	9 (11.8%)	0	0
	Total	107	82 (76.6%)	32 (29.9%)	50 (46.7%)	4 (3.7%)	19 (18%)	2 (1.9%)	0
2016	+Ve	25	15 (60%)	8 (32%)	7 (28%)	2 (8%)	6 (24%)	0	2 (8%)
	–Ve	50	30 (60%)	21 (42%)	22 (38%)	3 (6%)	4 (8%)	0	0
	Total	75	45 (60%)	29 (36.7%)	29 (36.7%)	5 (6.7%)	10 (13.3%)	0	2 (2.7%)
Total		544	406 (74.6%)	175 (32.2%)	231 (42.5%)	38 (7%)	73 (13.4%)	3 (0.6%)	10 (1.8%)

TSR – treatment success rate

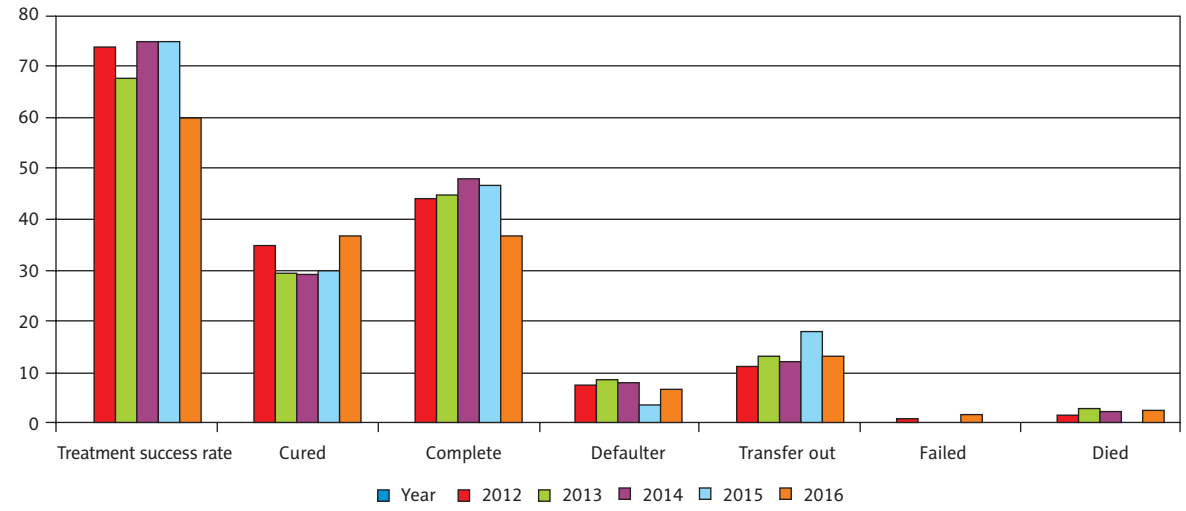

Fig. 1. Outcome of tuberculosis treatment among five years in Arba Minch General Hospital, Arba Minch, Southern Ethiopia 2012 to 2016

and default (COR = 1.37; 95% CI: 0.669-2.825) when compared with the HIV-negative patients (Table 3).

Discussion

In the present study, the prevalence of HIV co-infection among TB patients was 29.2%, similar to the studies conducted in northwest Ethiopia (25%) [13]. However, this finding is higher than that of a study conducted in northwest Ethiopia (11.4%)[14], a 2016 WHO report for Ethiopia (10%) [2], for Brazil (19%) [15] and for Nigeria (20%) [16].

Overall, TSR of registered TB patients with and without HIV was 74.6%, which is inconsistent with the WHO target of 85% [9] and EMoH target of 97% [7]. However, our finding is consistent with the previous report for Tigray [17], Gondor [18] and western Ethiopia [19]. The TSR was worse in tuberculosis patients with HIV than without HIV. In the present study, HIV-seropositive TB patients had higher odds of failure, transfer out and default as compared

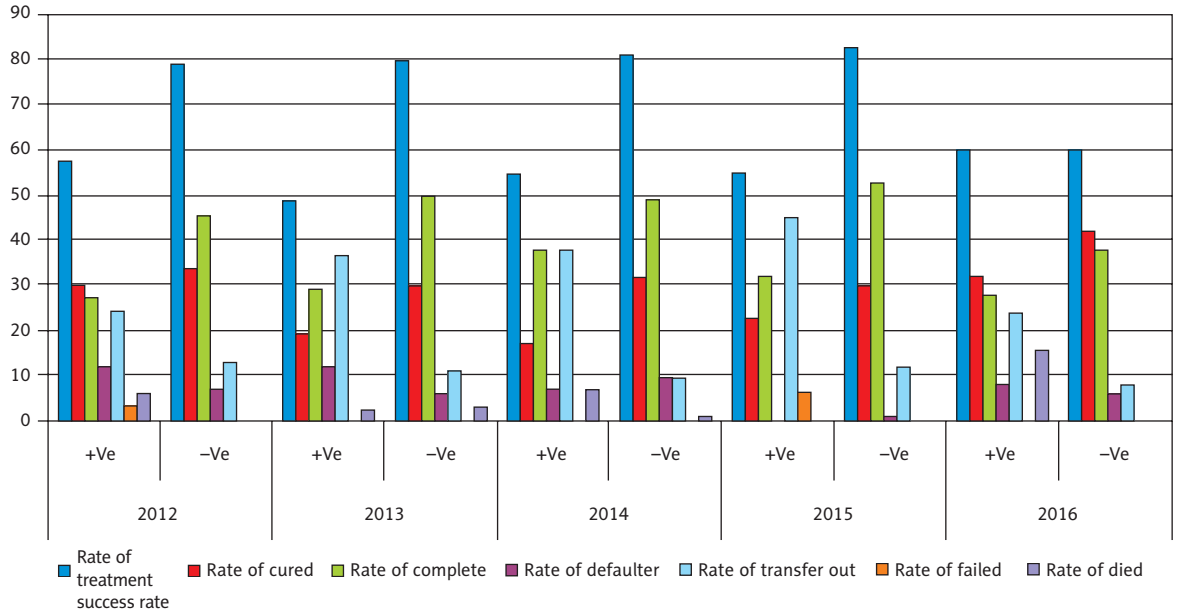

Fig. 2. Comparison of HIV+ and HIV– in terms of tuberculosis treatment outcome in tuberculosis patients treated at Arba Minch General Hospital, 2012 to 2016

Table 3. Results of logistic regression analysis for predictors of the tuberculosis treatment outcome, Arba Minch Hospital, 2012-2016

Variable	Crude odds ratio (95% confidence interval)				
	Cured/completed	Defaulter	Failed	Deaths	Transfer out
HIV+ VS HIV-	1 reference	1.37 (0.669-2.825), $p = 0.385$	20.79 (1.065-406.01), $p = 0.045$	6.95 (1.765-27.394), $p = 0.005$	2.59 (1.557-4.334), $p = 0.0003$

*HIV+ – human immunodeficiency virus; *Cured + completed = treatment success*

to those of HIV sero-negatives. The mortality rate in TB/HIV-positive patients was higher than in HIV-negative patients. Those who were HIV positive had about 7 times higher odds of death and threefold higher odds of transfer out to other health institutions compared with HIV-negative TB patients. This finding is slightly lower than the research conducted in Arsi Negelle Health Center [11], Addis Ababa [20], Tigray [21], central Ethiopia [22], south Ethiopia [23, 24], and northwest Ethiopia [10, 13, 25], while this result is higher relative to a study in Northwest Ethiopia [25], Northern Ethiopia [26], west Gojjam [27], and Southwest Ethiopia [28]. The possible reason for the observed difference might be differences in study population, high number of transfer-out cases [25] and increased number of unrecorded treatment outcomes in the study in south Ethiopia [23, 24].

The HIV sero-positive patients were more likely to be transferred out to other health institutions [11] as compared to the HIV-negative patients [10], which could have an adverse effect on evaluation of TB treatment outcomes because this group was included in the denominator [11]. In addition to this, the feedback system is poor and there are no ways to determine whether these patients registered to continue treatment in another health center [25]. The possible reason for transfer out of these patients may be due to lack of confidentiality associated with HIV testing or fear of disgrace associated with accessing ART. This might be an issue which needs improvements and consultancy. Although studies have shown that patients who default tend to be at higher risk of TB treatment failure (develop MDR-TB) associated with a longer period of TB transmission in the community and had a higher rate of mortality [22, 29], still there are different factors that cause the patients from developing countries to interrupt their treatment [30]. In this study, HIV-seropositive patients had about 2 times higher odds of defaulting and about 21 times higher odds of treatment failure [10, 11, 23]. This result partly indicates that HIV status [31] and being on ART [32] were factors associated with TB treatment non-adherence and lost-to-follow-up. Also our finding showed that the risk of death was significantly higher among HIV-positive TB patients than HIV-negative patients, which agrees with findings from previous studies [11, 23, 26, 27]. A number of possible explanations have been proposed for the striking difference in mortality between patients with tuberculosis only and those co-infected with HIV. Several immunological studies, from different parts of the world, have

shown that the host responses to *Mycobacterium tuberculosis* facilitate HIV replication [33], thus accelerating the natural progression of HIV and further depressing cellular immunity. This contributes to late presentation and diagnosis of HIV [34], which indicate that HIV-seropositive TB patients have been implicated in the increased mortality. Also the difficulty of TB diagnosis and the consequent delay in treatment initiation may result in higher mortality among PTB and extrapulmonary tuberculosis (EPTB) patients [35].

Conclusions

This study showed that the successful anti-TB treatment outcome among TB/HIV co-infected patients who attended their treatment at the Arba Minch General Hospital TB DOTS clinic was below the target set by WHO and Ethiopian Ministry of Health. Also, we were able to demonstrate from our data that HIV-negative patients being treated for TB were associated with better treatment outcome. We conclude that treatment plans that emphasize DOTS for at-risk patients have the greatest success in improving tuberculosis treatment outcome in the region. Urgently strengthening the coordinated tuberculosis control program and treatment outcome monitoring is strongly recommended. Thus, we recommended that strengthening the integration of TB/HIV collaborative activities could improve the treatment outcome. In addition, to improve TB patients' follow-up, it is better to keep them in contact with nearby health professionals.

Our study shares the inherent limitation of a retrospective study and may be subjected to random error and selection bias. As this study was based on a retrospective review of TB registers, comprehensive analysis of all relevant risk factors such as treatment adherence, CD4+ count, opportunistic infections, timing of ART, ART enrollment and provision of current procedural terminology CPT do not routinely capture from the record, which may overestimate or underestimate the impact of HIV status on TB treatment outcome.

Acknowledgements

I acknowledge the technical support provided by AMH. My special thanks and appreciation also go to the AMH administration, who gave permission for this paper's publication.

Conflict of interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

References

1. World Health Organization, Global TB report 2012, WHO office. WHO, Geneva 2012.
2. World Health Organization, Global tuberculosis report 2016. WHO, Geneva 2016.
3. Shaweno D, Worku A. Tuberculosis treatment survival of HIV positive TB patients on directly observed treatment short-course in Southern Ethiopia: a retrospective cohort study. BMC Res Notes 2012; 5: 682.
4. Sileshi B, Deyessa N, Girma B, et al. Predictors of mortality among TB-HIV co-infected patients being treated for tuberculosis in Northwest Ethiopia: a retrospective cohort study. BMC Infect Dis 2013; 13: 297.
5. Gray JM, Cohn DL. Tuberculosis and HIV coinfection. In: Seminars in respiratory and critical care medicine. Thieme Medical Publishers, 2013.
6. Federal Ministry of Health. Tuberculosis, Leprosy and TB/HIV Prevention and Control Programme. Addis Ababa, 2008; 207.
7. Federal Ministry of Health of Ethiopia. Manual of Tuberculosis, Leprosy and TB/HIV prevention and control programme. Addis Ababa, 2008.
8. Federal Ministry of Health of Ethiopia. Tuberculosis Annual Bulletin. Addis Ababa, 2010.
9. World Health Organization. Global tuberculosis report 2014. WHO, Geneva 2014.
10. Cheru F, Mekonen D, Girma D, et al. Comparison of treatment outcomes of tuberculosis patients with and without HIV in Gondar University Hospital: a retrospective study. J Pharm Biomed Sci 2013; 34: 1606-1612.
11. Gebremariam G, Asmamaw G, Hussen M, et al. Impact of HIV Status on Treatment Outcome of Tuberculosis Patients Registered at Arsi Negele Health Center, Southern Ethiopia: A Six Year Retrospective Study. PLoS One 2016; 11: e0153239.
12. World Health Organization. Treatment of tuberculosis: guidelines. WHO, Geneva 2010.
13. Biadglegne F, Wubie BA, Debebe T, et al. A retrospective study on the outcomes of tuberculosis treatment in Felege Hiwot Referral Hospital, Northwest Ethiopia. Int J Med Med Sci 2013; 5: 85-91.
14. Tadesse S, Tadesse T. HIV co-infection among tuberculosis patients in Dabat, northwest Ethiopia. J Infect Dis Immun 2013; 5: 29-32.
15. do Prado TN, Miranda AE, de Souza FM, et al. Factors associated with tuberculosis by HIV status in the Brazilian national surveillance system: a cross sectional study. BMC Infect Dis 2014; 14: 415.
16. Babatunde OA, Elegbede OE, Ayodele M, et al. Factors affecting treatment outcomes of tuberculosis in a tertiary health center in Southwestern Nigeria. Int Rev Soc Sci Hum 2013; 4: 209-218.
17. Belayneh M, Giday K, Lemma H. Treatment outcome of human immunodeficiency virus and tuberculosis co-infected patients in public hospitals of eastern and southern zone of Tigray region, Ethiopia. Braz J Infect Dis 2015; 19: 47-51.
18. Sinshaw Y, Alemu S, Fekadu A, et al. Successful TB treatment outcome and its associated factors among TB/HIV co-infected patients attending Gondar University Referral Hospital, Northwest Ethiopia: an institution based cross-sectional study. BMC Infect Dis 2017; 17: 132.
19. Ejeta E, Birhanu T, Wolde T. Tuberculosis treatment outcomes among tuberculosis/human immunodeficiency co-infected cases treated under directly observed treatment of short course in Western Ethiopia. J AIDS HIV Res 2014; 6: 164-171.
20. Getahun B, Ameni G, Medhin G, et al. Treatment outcome of tuberculosis patients under directly observed treatment in Addis Ababa, Ethiopia. Braz J Infect Dis 2013; 17: 521-528.
21. Berhe G, Enquselassie F, Aseffa A. Treatment outcome of smear-positive pulmonary tuberculosis patients in Tigray Region, Northern Ethiopia. BMC Public Health 2012; 12: 537.
22. Hamusse SD, Demissie M, Teshome D, et al. Fifteen-year trend in treatment outcomes among patients with pulmonary smear-positive tuberculosis and its determinants in Arsi Zone, Central Ethiopia. Glob Health Action 2014; 7: 25382.
23. Muñoz-Sellart M, Cuevas LE, Tumato M, et al. Factors associated with poor tuberculosis treatment outcome in the Southern Region of Ethiopia. Int J Tuberc Lung Dis 2010; 14: 973-979.

24. Shargie EB, Lindtjørn B. Determinants of treatment adherence among smear-positive pulmonary tuberculosis patients in Southern Ethiopia. PLoS Med 2007; 4: e37.
25. Tessema B, Muche A, Bekele A, et al. Treatment outcome of tuberculosis patients at Gondar University Teaching Hospital, Northwest Ethiopia. A five-year retrospective study. BMC Public Health 2009; 9: 371.
26. Endris M, Moges F, Belyhun Y, et al. Treatment outcome of tuberculosis patients at Enfraz Health Center, Northwest Ethiopia: a five-year retrospective study. Tuberc Res Treat 2014; 2014: 726193.
27. Gebreegziabher SB, Yimer SA, Bjune GA. Tuberculosis case notification and treatment outcomes in West Gojjam Zone, Northwest Ethiopia: a five-year retrospective study. J Tuberculosis Res 2016; 4: 23-33.
28. Fiseha T, Gebru T, Gutema H, et al. Tuberculosis treatment outcome among HIV co-infected patients at Mizan-Aman general hospital, Southwest Ethiopia: a retrospective study. Journal of Bioengineering & Biomedical Sciences 2015; 5: 1.
29. Tekle B, Mariam D, Ali A. Defaulting from DOTS and its determinants in three districts of Arsi Zone in Ethiopia. Int J Tuberc Lung Dis 2002; 6: 573-579.
30. Tola HH, Tol A, Shojaeizadeh D, et al. Tuberculosis treatment non -adherence and lost to follow up among TB patients with or without HIV in developing countries: a systematic review. Iran J Public Health 2015; 44: 1-11.
31. Ngamvithayapong J, Winkvist A, Diwan V. High AIDS awareness may cause tuberculosis patient delay: results from an HIV epidemic area, Thailand. AIDS 2000; 14: 1413-1419.
32. Gebremariam MK, Bjune GA, Frich JC. Barriers and facilitators of adherence to TB treatment in patients on concomitant TB and HIV treatment: a qualitative study. BMC Public Health 2010; 10: 651.
33. Falvo JV, Ranjbar S, Jasenosky LD, et al. Arc of a vicious circle: pathways activated by Mycobacterium tuberculosis that target the HIV-1 long terminal repeat. Am J Respir Cell Mol Biol 2011; 45: 1116-1124.
34. Ifebunandu NA, Ukwaja KN, Obi SN. Treatment outcome of HIV-associated tuberculosis in a resource-poor setting. Tropical Doctor 2012; 42: 74-76.
35. Sanchez M, Bartholomay P, Arakaki-Sanchez D, et al. Outcomes of TB treatment by HIV status in national recording systems in Brazil, 2003-2008. PLoS One 2012; 7: e33129.