Tuberculosis (TB) in the Refugee Camps in Ethiopia: Trends of Case Notification, Profile, and Treatment Outcomes, 2014 to 2017

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Abstract

Background: Severity of TB increases in refugee populations. Monitoring TB case notification and treatment outcomes are essential to evaluate the effectiveness of TB programs. This study aimed to determine trends in TB case notification and treatment outcomes and explore factors associated with unsuccessful treatment outcome in refugee camps in Ethiopia.

Methods: This retrospective cohort study was conducted from October 2018-June 2019. Demographic and clinical data of all TB cases registered from 2014 to 2017 in 25 refugee camps located in seven refugee areas *(Shire, Afar, Gambella, Asossa, Mizam, Jijiga, and Dollo Ado)* were extracted using pre-tested data extraction format. Multivariate logistic regression was performed to calculate odds ratios and 95% confidence intervals for factors associated with unsuccessful outcomes.

Results. A total of 1553 TB cases, mean age 27.7 years, were registered (2014-2017). Of these notified cases 54.7% were men, 27.7% children (< 15 years), 71.2% pulmonary TB (PTB), 27.8% Extra-PTB (EPTB) and 98.3% new and relapse. From 2014 to 2017: there was consistent increase in the number of notified TB cases (138 to 588 cases), in the percentage of EPTB (23.2% to 32.7%), bacteriologically confirmed pulmonary new and relapse (43.8% to 64.8%), and contribution of children to total TB cases (18.8% to 30.1%) and to EPTB (40.6% to 65.1%). Treatment success rates for all TB cases remained lower at 72.7%-79.4% (on average 11.7% were not evaluated, 8.0% lost to follow-up (LTFU), 4.8% died, and 0.5% failed). Unsuccessful treatment was significantly associated with pretreatment weight below 40 Kg, age over 45 years, and being HIV positive.

Conclusions: This study has provided valuable evidences that can help to improve the TB programs. There was increased trend in number of notified TB cases, and in proportion of EPTB, childhood TB, and bacteriologically confirmed pulmonary new and relapse cases. Treatment success rate (2014-2017) was far below global target (90%), and “not evaluated” and LTFU treatment outcomes were higher, which need to be improved. Special socio-economic support and monitoring is required for patients with pretreatment weight below 40 Kg, age over 45 years and HIV positives who at risk for unsuccessful treatment.

1. Background

Tuberculosis (TB) is an ancient infectious disease caused primarily by *Mycobacterium tuberculosis* (*MTB*) [1]. Despite that significant global success achieved to control TB in the past 20 years (58 million lives have been saved since 2000), TB is one of the top ten causes of death, and is the leading cause of death from single infectious agent above HIV/AIDS. Globally in 2018, there were an estimated 10 million incident TB cases, 1.5 million deaths from TB, and 0.5 million people fell ill with drug resistant TB. In addition, 8.6% of TB cases in the world were living with HIV, of whom 72% were in Africa [2].

However, due to poor shelter and living conditions, poor health and nutritional status, overcrowding, and inadequate access to TB care and prevention, the burden and severity of TB is higher in migrants, refugees and displaced populations (DPs) [3–6]. Moreover, the risk of acquiring multi-drug resistant

(MDR) TB and unsuccessful TB treatment outcome is higher among refugees [7, 8]. In order to end to TB by 2030, therefore, strengthen TB care and prevention in refugee and displaced population has been listed as one of the ten components of the End TB strategy by world health organization (WHO) [2].

Ethiopia, a country with population size of 109 million, is among the 30 high burden countries for TB, TB/HIV and MDR-TB. By 2018, the estimated total TB incident, notified TB cases and TB mortality in Ethiopia was 165000, 114 233 and 24 000, respectively [2]. Nevertheless, Ethiopia hosts more than 700,000 refugees in 26 refugee camps by 2019. Majority of the refugees are from South Sudan, Somalia, Eritrea and Sudan where TB is predominant. Together, the occurrence of high TB burden in the host and source countries, the large refugee population in the host country, as well as the intrinsic vulnerability of the refugee population to TB can potentially attribute to increase the burden and severity of TB in the refugee populations in Ethiopia [3, 4, 5, 6, 9]. Therefore, in order to improve the effectiveness of TB programs in the refugee camps, the performance of the TB programs need to be evaluated and monitored regularly. Among the main indicators for TB program performance are TB case finding, notification, and treatment outcome **[10. 11]**.The aim of this study was to determine trends on TB case notification, profile and treatment outcome, and explore factors associated with unsuccessful TB treatment outcomes in the refugee camps in Ethiopia in the past four years (2014–2017).

2. Materials And Methods

2.1. Study settings

This study was conducted in 25 refugee health facilities/refugee camps which are located in seven refugee areas in Ethiopia. The list of refugee areas, refugee camps and health facilities is presented in **supplement 1**. In Ethiopia, there are nine regional states and two administrative cities. In the country, there are 26 refugee camps sub-organized in seven refugee areas *(Shire, Afar, Gambella, Asossa, Mizam, Jijiga, Dollo Ado)* which are located in six regional states. 1) Shire refugee area: north west of the country in Tigray region, hosts four refugee camps, 2) Afar refugee area: east of the country in Afar region, hosts two refugee camps, 3) Gambella refugee area: west of the country in Gambella Region, hosts six refugee camps, 4) Mizan refugee area: south of the country in Southern nations and nationalities Region, hosts one refugee camps, 5) Asossa refugee area: west of the country in Asossa region, hosts four refugee camps, 6) Jijiga and 7) Dollo Ado refugee areas, east of the country in Somalia region, hosts three and five refugee camps, respectively. In each refugee camp, there is health facility which deliver general health services including TB diagnostic and/or treatment services to the refugee population.

The total end year refugee population in Ethiopia was continuously increased from 491030 in 2014 to 728000 by 2017. The highest refugee population by 2017 were in Gambella (219,708), followed by Dollo Ado (197.952), Shire (109, 360), Asossa (55.726), Jijiga (35,024), Afar (15.390), and Mizan (11,761) refugee areas [12].

Therefore, based on the inclusion critrea (heatlh facilites which have both TB diagnosis and treatment servces starting at least in 2017), this study was conducted in 25 health facilities (HFs)/25 refugee camps located in seven refugee areas (4 HFs in Shire, 2 HFs in Afar, 6HFs in Gambella, 1 HF in Mizan, 4 HFs in Asossa, 3 HFs in Jijiga, and 5 HFs in Dollo Ado) **(Supplement 1)**. All health facilities included in the study had standardized unit TB registers.

2.2. Study design, population, and data collection

This four year (2014–2017) health facility based retrospective cohort study was conducted from October 2018 to June 2019. The study population were all refugee TB patietns registered from 2014 to 2017 in the 25 refugee health facilities. For each study participant, demographic and clinical data were extracted from Unit TB patient register by trained health officers and nurses using a pre-tested data extraction format. To ensure data quality, training was given to data collectors, study coordinators and supervisors; supervision was done on daily basis during data collection; and then 10% of the data were randomly selected by the study coordinators and were re-collected by the field supervisors and were checked page by page.

2.3. Data entry and statistical analysis

Data were coded and double entered by two trained data clerks using Epi-info version 7 and then cross-checked for consistency. Data were exported to STATA version 13 (Stata Corp, College Station, TX, USA) for data checking, cleaning, and analysis. During the preliminary analysis we looked for errors and corrected them by re-checking the data collection Forms. Descriptive analysis (frequency, mean and standard deviation) were analysed. Binary logistic regression analysis was done to identify independent variables associated with unsuccessful treatment outcome. Finally, multivariate logistic regression analysis was used to measure the independent effects of each predictor variable on unsuccessful treatment outcomes. Variables with a P-value of < 0.05 in the bivariate analysis were included in the multivariate model. The independent variables used were age, sex, baseline weight, type of TB, category of TB patient, HIV infection and ART status. Statistical significance level was considered at a P-value < 0.05. Odds ratios with 95% confidence interval (CI) were used to assess the strength of association between variables.

Definitions

TB case definition and TB treatment outcomes were defined according to the standard definitions in the National guidelines for TB in Ethiopia [10] and and WHO guideline [11].

- **TB case notification**: is where TB is diagnosed in a patient and is reported within the national TB surveillance system.
- **TB cases**: is a patient in whom TB has been diagnosed.
- **A bacteriologically confirmed TB case**: is one from whom a biological specimen is positive by smear microscopy, culture or WHO approved rapid diagnostics (such as Xpert MTB/RIF); and

- **Clinically diagnosed TB case**: is one who does not fulfil the criteria for bacteriological confirmation but has been diagnosed with active TB by a clinician or other medical practitioner who has decided to give the patient a full course of TB treatment.
- **Extra pulmonary tuberculosis (EPTB)**: any bacteriologically confirmed or clinically diagnosed **case of TB** involving organs other than the lungs; and
- **Pulmonary tuberculosis (PTB)**: any bacteriologically confirmed or clinically diagnosed **case of TB** involving the lung parenchyma or the tracheobronchial tree.

  Pulmonary TB positive (PTB+): Bacteriologically confirmed pulmonary TB cases using available confirmatory diagnostic methods; and
  Pulmonary TB negative (P/Neg): Clinically diagnosed pulmonary TB cases.

Patients were classified into two groups according to their TB treatment history:

1. **New TB patients**: are those who have never been treated for TB or have taken anti-TB drugs for less than 1 month;
2. **Previously treated TB patients**: are those who have received one month or more of anti-TB drugs in the past, and were categorized further as:

Relapse patients

are those who have previously been treated for TB, were declared cured or treatment completed at the end of their most recent course of treatment, and are now diagnosed with a recurrent episode of TB (either a true relapse or a new TB caused by reinfection);

Treatment after failure patients

are those who have previously been treated for TB and whose treatment failed at the end of their most recent course of treatment;

Treatment after loss to follow-up patients

are those who have previously been treated for TB and were declared lost to follow-up at the end of their most recent course of treatment. *(These were previously known as treatment after default patients);*

Other previously treated patients

are those who have previously been treated for TB but whose outcome after their most recent course of treatment is unknown or undocumented;

Transfer in

A patient who started treatment in one health facility (reporting unit) and transferred to another health facility (reporting unit) to continue treatment.

- **Treatment outcomes were categorised as follows**:

Cured

A pulmonary TB patient with bacteriologically confirmed TB at the beginning of treatment who was smear- or culture-negative in the last month of treatment and on at least one previous occasion;

Treatment Completed

A TB patient who completed treatment without evidence of failure **BUT** with no record to show that sputum smear or culture results in the last month of treatment and on at least one previous occasion were negative either because tests were not done or because results are unavailable;

Treatment failed

A TB patient whose sputum smear or culture is positive at month 5 **or** later during treatment;

Lost to follow up

A TB patient who did not start treatment **or** whose treatment was interrupted for 2 consecutive months or more;

Died

A TB patient who dies for any reason before starting **or** during the course of treatment;

Not evaluated

A TB patient for whom no treatment outcome is assigned. This includes cases “transferred out” to another treatment unit as well as cases for whom the treatment outcome is unknown to the reporting unit.

Successful treatment outcome

cured and treatment completed) and ;

Unsuccessful treatment outcome

died, treatment failed and lost to follow up.

3. Results

3.1. General characteristics of the study population

From 2014 to 2017, a total of **1553 TB cases** of whom 1108 (72.0%) PTB, 431 (28.0%) EPTB, and1527 (98.8%) new and relapse cases were registered in 25 refugee camps in Ethiopia. Among the PTB cases, 677 (61.1%) were smear positive (PTB+), 426 (38.4%) were smear negative, and 5 (0.5%) were smear not done. Among the 1527 new and relapse cases, 1093 (70.4%) were pulmonary new and relapse, of whom 666 (60.9%) were bacteriologically confirmed and 427 (39.1%) were clinically diagnosed. Of the total TB cases registered, 850 (54.7%) were male and 690 (44.4%) were female. The mean age of the patients was 27.2 years. Children under 15 years and adults 15–44 years old represented 430 (27.7%) and 998 (52.4%) of the total patients registered, respectively. The clinical and sociodemographic characteristics of the TB cases is shown in Table 1.

Of the total 1553 TB cases notified during the study period, 858 (55.2%) were from Gambella area and 221 (14.2%) were from Dollo Adoa. The remaining Afar, Asossa, Mizan, and Shire refugee areas contributed 3.4%, 4.7%, 5.1% and 6.6% of the total TB cases notified, respectively. The number of notified TB cases for each refugee area and refugee health facility/refugee camp are presented in **Supplement 1.**

Table 1
Sociodemographic and clinical characteristics of the notified TB cases (n = 1553) among the refugee camps in Ethiopia, 2014–2017.

Characteristic	**2014, N (%)**	**2015, N (%)**	**2016 , N (%)**	**2017, N (%)**	**Total N (%)**
Total TB cases of all Forms	138	354	473	588	1553
Age group					
< 15	26 (18.8)	92 (26.0)	135 (28.5)	177 (30.1)	430 (27.7)
15–29	50 (36.2)	107 (30.2)	141 (29.8)	152 (25.9)	450 (29.0)
30–44	39 (28.3)	87 (24.6)	107 (22.6)	132 (22.4)	365 (23.5)
45–59	15 (10.9)	43 (12.1)	46 (9.7)	79 (13.4)	183 (11.8)
>= 60	6 (4.3)	23 (6.5)	39 (8.3)	44 (7.5)	112 (7.2)
Not documented	3 (2.2)	2 (0.6)	4 (1.0)	4 (0.7)	13 (0.8)
Mean age, years	28.0	27.1	26.8	27.0	27.2
Sex					
Male	80 (58.0)	193 (54.5)	247 (52.2)	330 (56.1)	850 (54.7)
Female	57 (41.3)	160 (45.2)	222 (46.9)	251 (42.7)	690 (44.4)
Not documented	1 (0.7)	1 (0.3)	4 (0.9)	7 (1.2)	13 (0.8)
Type of TB					
PTB**	106 (76.8)	279 (78.8)	334 (70.6)	389 (66.2)	1108 (71.3)
EPTB	32 (23.2)	73 (20.6)	134 (28.3)	192 (32.7)	431 (27.8)
Not documented	0	2 (0.6)	5 (1.1)	7 (1.1)	14 (0.9)

PTB+: Smear-positive pulmonary TB; **P/Neg**: Smear-negative pulmonary TB

***New and relapse**: includes cases for which the treatment history is unknown (not recorded) and transfer in; and it excludes cases that have been re-registered as *treatment after failure*, as *treatment after lost to follow up* or as *other previously treated with unknown or undocumented treatment outcome*

** **PTB**: includes PTB+, P/Neg, and Smear not done

Characteristic	2014, N (%)	2015, N (%)	2016 , N (%)	2017, N (%)	Total N (%)
Type of TB by diagnostic category					
PTB+	47 (34.0)	162 (45.8)	216 (45.7)	252 (42.9)	677 (43.6)
P/Neg	59 (42.8)	116 (32.8)	118 (25.0)	133 (22.6)	426 (27.4)
Pulmonary Smear not done	0	1 (0.3)	0	4 (0.7)	5 (0.3)
EPTB	32 (23.2)	73 (20.6)	134 (28.3)	192 (32.6)	431 (27.8)
Not documented	0	2 (0.5)	5 (1.0)	7 (1.2)	14 (0.9)
TB patient by previous treatment history:					
New and relapse*	137 (99.3)	347 (98.0)	462 (97.7)	581 (98.8)	1527 (98.3)
Treatment after Failure	0	0	1 (0.2)	1 (0.2)	2 (0.1)
Lost to Follow up to Treatment	1 (0.7)	3 (0.8)	5 (1.1)	4 (0.6)	13 (0.8)
Others	0	1 (0.3)	2 (0.4)	1 (0.2)	4 (0.3)
Not documented	0	3 (0.8)	3 (0.6)	1 (0.2)	7 (0.5)
PTB: New and relapse	105 **(76.6)**	276 **(80.4)**	328 **(71.0)**	384 **(66.1)**	**1093 (71.6)**
bacteriologically confirmed cases:	46 (43.8)	161 (58.3)	210 (64.0)	249 (64.8)	666 (60.9)
Clinically diagnosed cases:	59 (56.2)	115 (41.7)	118 (36.0)	135 (35.2)	427 (39.1)
TB case by HIV status					
Positive	10 (8.6)	48 (15.3)	50 (13.2)	57 (10.9)	165 (10.6)
Negative	106 (91.4)	265 (84.7)	329 (86.8)	464 (89.1)	1164 (75.0)
Not documented	22 (15.9)	41 (11.6)	94 (26.6)	67 (11.4)	224 (14.4)

PTB+: Smear-positive pulmonary TB; **P/Neg**: Smear-negative pulmonary TB

***New and relapse**: includes cases for which the treatment history is unknown (not recorded) and transfer in; and it excludes cases that have been re-registered as *treatment after failure*, as *treatment after lost to follow up* or as *other previously treated with unknown or undocumented treatment outcome*

** **PTB**: includes PTB+, P/Neg, and Smear not done

Characteristic	2014, N (%)	2015, N (%)	2016 , N (%)	2017, N (%)	Total N (%)
ART initiation	4 (40.0)	44 (91.7)	38 (76.0)	48 (84.2)	134 (81.2)
Yes	6 (60.0)	4 (8.3)	12 (24.0)	9 (15.8)	31 (18.8)
No					
TB cases by refugee areas	21 (15.2)	28 (7.9)	26 (5.5)	28 (4.8)	103 (6.6)
Shire	0	0	6 (1.3)	47 (8.0)	53 (3.4)
Afar	43 (31.2)	159 (44.9)	288 (60.9)	368 (62.6)	858 (55.2)
Gambella	2 (1.4)	30 (8.5)	18 (3.8)	29 (4.9)	79 (5.1)
Mizan	14 (10.1)	29 (8.2)	16 (3.4)	14 (2.4)	73 (4.7)
Asossa	45 (32.6)	42 (11.9)	45 (9.5)	34 (5.8)	166 (10.7)
Jijiga	13 (9.4)	66 (18.6)	74 (15.6)	68 (11.6)	221 (14.2)
Dollo Ado					
PTB+: Smear-positive pulmonary TB; **P/Neg**: Smear-negative pulmonary TB					
***New and relapse**: includes cases for which the treatment history is unknown (not recorded) and transfer in; and it excludes cases that have been re-registered as *treatment after failure*, as *treatment after lost to follow up* or as *other previously treated with unknown or undocumented treatment outcome*					
** **PTB**: includes PTB+, P/Neg, and Smear not done					

3.2. Overall trends in TB case notification, 2014 to 2017

Trends in case notification by type of TB and treatment history

From 2014 to 2017: the number of notified TB cases of all forms has increased from 138 to 588 cases. Among these total notified cases, the percentage of EPTB increased from 23.2–32.7%, while PTB decreased from 76.8–66.2%. Among the PTB cases, the percentage of smear-positive pulmonary TB (PTB+) increased from 44.3–64.8%, smear-negative pulmonary TB (P/Neg) was declined from 55.7–34.2%, and smear not done was remained lower (0.3%-1.0%) **(**Table 1**).** Among the pulmonary new and relapse cases, those bacteriologically confirmed have increased from 43.8% in 2014 to 64.8% in 2017, and those clinically diagnosed have declined from 56.2–35.2%.

By treatment history, 97.7%-99.0% of the TB patients registered during the study period were new and relapse; whereas on average 0.1%, 0.8%, 0.3% and 0.5%, respectively, were treatment after failure, lost to follow up to treatment, and “others” **(**Table 1**)**.

Trends in cases notification segregated by gender

The number of notified cases for both men and women increased from 2014 to 2017, but predominated by men. For men it was increased from 80 to 330 cases and for women from 57 to 251 cases (Table 1). The average number of notified cases for men was 213 (standard deviation, SD = 105), whereas that for women was 173 (SD = 86) (two-sample t test, P = 0.39). Likewise, the proportion of notified cases was predominated by men over the study period (> 52%), with the male-to-female (M:F) notification ratio consistently > 1.1:1. However, the M:F ratio was declined from 1.4 in 2014, 1.2 in 2015, to 1.1 in 2016, and then increased to 1.3 in 2017 (Table 1).

Trends in case notification segregated by age category

There was a variation in TB case notification by age category. Patients in the age group 15–44 years were predominantly contributed 815 cases (52.5%) of the total TB cases notified, followed by children (< 15 years) which constituted 430 cases (27.7%). For every year during the study period, patients in the < 15, 15–29, 30–44, 45–59, and above 60 age groups contributed an average of 27.7%, 29.0%, 23.5%, 11.8%, and 7.2%, respectively, of the total cases notified (Table 1).

However, from 2014 to 2017, the contribution of age groups 15–44 years to the total TB cases was decreased from 64.9–48.3%, whereas the contribution of children (< 15 years) was increased from 18.8–30.1%, and that of above 45 years was increased from 4.4–7.5% (Table 1, Fig. 1).

Compared to the other age categories, the share of children (< 15 years) to EPTB cases was continuously increased and remained at highest level over the years. Thus, of the total EPTB cases notified in 2014, 2015, 2016 and 2017, 40.6%, 45.2%, 58.2%, and 65.1%, respectively, were children under 15 years old.

Figure 1. **Total TB case notified in the refugee camps in Ethiopia disaggregated by age category, 2014 to 2017**

TB case notification segregated by age group and sex

The percentage of notified TB cases for men was higher (> 50%) than for women in all the age categories (< 15, 15–29, 30–44, 45–59 and > 60 years old) across the years (2014–2017), except for age 60, < 15 and 30–44 years in 2014, 2015 and in 2017, where men constituted 50%, 49.5%, and 49.2%, respectively (Fig. 2).

Figure 2. **TB cases notified in the refugee camps in Ethiopia by age group and sex, 2014 to 2017.**

3.3. Trends in HIV testing and antiretroviral treatment coverage

HIV testing was performed in 1329 (85.6%) of the 1553 notified cases, among those 165 (12.4%) were HIV positive (Table 1). The percentage of TB patients tested for HIV was increased from 84.1% in 2014 to 88.6% in 2017. The percentage of TB patients tested HIV positive was decreased from 15.3% in 2015 to

10.9% in 2017, whereas antiretroviral treatment (ART) coverage increased from 40% in 2014 to 84.2% in 2017 (Table 1).

3.4. Trends in TB Treatment outcomes, 2014 to 2017

Treatment outcome was evaluated for a total of 1553 TB cases of all forms (Table 2) and for new and relapse TB cases (Fig. 3) registered from 2014 to 2017. The four year trend of treatment success rate for all TB cases was steady and remained lower at 72.4–79.4%. Cure has increased from 18.8% in 2014 to 27.7% in 2017; while the completed treatment rate has decreased from 56.5% in 2014 to 46.6% in 2017. Among the unsuccessful treatment outcomes, the rate for "not evaluated" was highest across the study period (8.5%-13.1%), followed by LTFU (5.6%-8.9%), died (3.6%-5.4%) and failed (0.2% -1.1%) (Table 2). Of the LTFU cases in 2016 and 2017, 56.1% and 78% % were males, respectively.

Treatment success rate for new and relapse TB cases from 2014 to 2017 remained stable and lower at 72.5%-80.1%. There was highest "not evaluated" (8.1%-13.4%) followed by LTFU (5.5%-8.9%), died (3.7%-5.2%), and failed (0-1.2%).

Table 2
Trends of TB treatment outcome for TB cases of all forms registered for treatment (n = 1553) among refugee camps in Ethiopia, 2014–2017.

Treatment outcomes	Years				
	2014, n (%)	**2015, n (%)**	**2016, n (%)**	**2017, n (%)**	**Total, n%**
Cured	26 (18.8)	75 (21.2)	119 (25.2)	163 (27.7)	383 (24.7)
completed	78 (56.5)	206 (58.2)	225 (47.5)	274 (46.6)	783 (50.4)
Failed	1 (0.7)	4 (1.1)	1 (0.2)	2 (0.3)	8 (0.5)
LTFU	11 (8.0)	20 (5.6)	42 (8.9)	51 (8.7)	124 (8.0)
Died	5 (3.6)	19 (5.4)	24 (5.1)	26 (4.4)	74 (4.8)
Not evaluated	17 (12.3)	30 (8.5)	62 (13.1)	72 (12.2)	181 (11.7)
Success rate	104 (75.3)	281 (79.4)	344 (72.7)	437 (74.3)	1166 (75.1)

Data are presented as numbers (%)

LTFU before treatment initiation

LTFU of smear positive PTB patients before starting treatment will have negative impact on clinical outcome and TB transmission. In the refugee camps, among TB cases who were smear positive PTB and registered in the laboratory log book in 2014, 2015, 2015 and 2017, respectively, 23 (29.1%), 22 (27.9%), 18 (22.8%), and 16 (20.3%) were not registered in the Unit TB register and treatment outcome was not recorded *(LTFU before treatment)*. Of the 16 LTFU before treatment in 2017, all were from Gambella refugee area, where 8 (50.0%) were from Kule, 5 (31.3%) from Terkedi, and 1 (6.2%) from Pugnido Agnewak refugee health facilities.

Treatment outcomes by gender, age, and type of TB

There was a variation in treatment success rate by gender, age category and type of TB (Fig. 3**)**. From 2015 to 2017, treatment success rate was relatively higher for females, but declined for both sexes (from 80.6–75.7% for female; from 78.2–73.6% for male) (Fig. 3A**).** Lowest treatment success rate was observed in the oldest age (60 + years old) over the study period, although it increased from 50.0% in 2014 to 65.9% in 2017. The treatment success rate was highest for children (< 15 years) in 2014 (80.8%) and 2015 (85.9%), but declined in 2016 (70.4%) and in 2017 (71.3%). Treatment success rate for the younger age group (15–29 years old) was remained stable (74.8%-78.9%) over the study period (Fig. 5B). Treatment success for PTB was higher over the years (except in 2015) than in EPTB, but declined gently from 2015 to 2017 in both groups **(**Fig. 3C**).**

Figure 3. **TB treatment success rate of the TB cases registered in the refugee camps in Ethiopia (2014–2017) by gender (A), age category (B), and by type of TB (C).**

3.5. Factors associated with unsuccessful TB treatment outcomes

Based on a **multivariate analysis**, factors associated with unsuccessful TB treatment outcome (LTFU, failure, and died) were pretreatment weight < 40 Kg (adjusted odds ratio [aOR] = 1.5, 95% confidence interval (CI): 0.9–2.3, *P = 0.05*); age 45–59 years (aOR = 2.4, 95% CI:1.3–4.7, *P = 0.008*); age > 60 years (aOR = 4.3, 95% CI:2.3–9.1, P < 0.001), and HIV infection (aOR = 3.6, 95% CI:2.3–5.8, *P < 0.001*) **(**Table 3**)**

Table 3
Factors associated with unsuccessful TB treatment outcomes among TB cases of all Forms in refugee camps in Ethiopia (2014– 2017)

Characteristics	**Successful outcomes**	**Unsuccessful outcomes**	**X^2, p-value**	**Bivariate analysis**		**Multivariate analysis**	
				OR (95%CI)	**P value**	**Adjusted OR (95% CI)**	**P value**
Gender	637 (84.3)	119 (15.7)	0.80;	1	0.74		
Male	522 (86.0)	85 (14.0)	0.37	1.04 (0.8–1.3)			
Female							
Age group	321 (86.5)	50 (13.5)	**33.7;**	1	0.8	2.4 (1.3–4.7)	**0.008**
< 15	349 (87.0)	52 (13.0)	**< 0.001**	0.9 (0.6–1.4)	0.3	4.3 (2.3–9.1)	**< 0.001**
15–29	286 (89.4)	34 (10.6)			**0.01**		
30–44	130 (77.8)	37 (22.16)		0.8 (0.5–1.2)	**0.001**		
45–59	72 (69.2)	32 (30.8)					
>= 60				1.8 (1.1–2.9)			
				2.8 (1.7–4.8)			
Pre-treatment weight, kg	576 (86.9)	87 (13.1)	**6.0;**	1	**0.08**	1.5 (0.9–2.3)	**0.05**
> 40	215 (80.5)	52 (19.5)	**0.01**	1.3 (0.9–1.8)			
< 40							
Type of TB	314 (82.6)	66 (17.4)	**6.5;**	1	**0.02**	0.6 (0.4-1.0)	**0.06**
P/Neg	528 (87.9)	73 (12.1)	**0.09**	0.6 (0.4–0.9)	0.8		
PTB+	4 (80.0)	1 (20.0)			0.8		
Smear not done	313 (83.2)	63 (16.8)		1.2 (0.1–10.8)			
EPTB				0.9 (0.6–1.4)			

* Odds ratio (OR) (95%CI) are based on 268 HIV positive study participants;

Characteristics	Successful outcomes	Unsuccessful outcomes	X^2, p-value	Bivariate analysis		Multivariate analysis	
Category of TB patients New and Relapse Failure LTFU Others(O)	1146 (85.0 2 (100) 8 (72.7) 3 (75.0)	202 (15.0) 0 3 (27.3) 1 (25.0)	**1.9;** **0.6**	1 2.1 (0.6–8.1) 1.8 (0.2–18.3)	0.2 0.6		
HIV status Negative Positive	934 (87.8) 102 (72.3)	130 (12.2) 39 (27.7)	**24.6;** **< 0.001**	1 1.6 (1.3-2.0)	**< 0.001**	3.6 (2.3–5.8)	**< 0.001**
ART initiated? * Yes No	89 (74.8) 148 (83.6)	30 (25.2) 29 (16.4)	**3.5;** **0.06**	1 0.9 (0.3-1.0)	**0.06**		
* Odds ratio (OR) (95%CI) are based on 268 HIV positive study participants;							

X^{2} = chi square;

P value < 0.05 was considered statistically significant.

4. Discussion

TB is more sever in refugee populations. This study provides evidences on TB case notification and treatment outcomes that can help to improve the effectiveness of the TB programs in the refugee camps in Ethiopia.

If high-performance of TB surveillance system is in place (e.g. with little under diagnosis and underreporting), TB case notification provides a good proxy indication for TB incidence [2]. In the refugee camps in Ethiopia, the number of notified TB cases was continuously increased from 138 in 2014 to 588 cases in 2017. Similarly, a study done in the refugee population in Gambella Region, Ethiopia, showed 29.0% increase in notified TB cases in eight years (2009–2017) [8], whereas another study done in Ethiopia showed a 90.4% increment in CNR of TB cases of all forms in 15 years (1997–2011) [12]. Although needs further investigation, there are four possible reasons that can explain the increased trend in TB case notification in the refugee camps: 1) real increase in TB incidence due to problems in the health care system that negatively affects the performance of TB programs (diagnosis, treatment and prevention), 2) surrounding community level factors that enhance TB transmission, 3) an increase in number of refugee population overtime, 4) progress in case detection and notification due to improvements in active case findings, diagnostic capacity, and recording and reporting system.

Evidence on TB epidemiology by type of TB (PTB and EPTB) will help to implement targeted TB diagnostic, treatment and prevention services. EPTB represented 32.7% of the total cases notified in the refugee camps in 2017. This is similar to the 31% EPTB cases among notified TB cases in Ethiopia in 2017 [13], but higher than the 15% EPTB among incident TB cases in the globe in 2018[2]. However, there was an increased trend in the proportion of EPTB in the refugee camps from 2014 (23.2%) to 2017 (32.7%). Together, our findings indicate a change in the epidemiology of EPTB in the refugee camps which suggests the need of further investigation to assess the possible confounding factors and to design targeted diagnostic, treatment and prevention strategies.

Evidences on the status of bacteriologically confirmed PTB, which is known as infectious TB, is essential to monitor resistance, disease severity, treatment response, and spread of TB. Limited access to health facilities and to diagnostic services, and low treatment success could contribute to high rate of TB transmissions and to higher smear positive PTB **(32).** Of the total new and relapse cases (incident TB cases) in the refugee camps in 2017, 66.2% were pulmonary cases, which is similar to the 66.9% for Ethiopia as reported by WHIO in 2018 [2]. Furthermore, of the pulmonary new and relapse cases in 2017 in the refugee camps, 64.8% were bacteriologically confirmed, which is higher than that for Ethiopia (58%) and for the globe (56%) as reported by WHIO 2018 [2]. Nonetheless, the proportion of bacteriologically confirmed pulmonary new and relapse cases in the refugee camps was increased from 43.8% in 2014 to 64.8% in 2017. This could be due to expansion of diagnostic services and an increase in the number and better utilization of bacteriologic diagnostics. However, the low proportion of bacteriological confirmed cases by 2017 (66.2%) can further be improved by refresher training and introduction and expansions of molecular diagnostics (sputum smear, molecular and culture).

TB affects both sexes but disproportionally males. Women face barriers to TB diagnosis and are less likely to report or show evidence of typical symptoms of pulmonary TB (cough, sputum production, and haemoptysis) [14, 15]. Despite that more than 70% of the refugees in the camps are women and children, males accounted 54.7% of the total notified TB cases. Similarly, 64% of the global and 57.3% of the national (Ethiopia) TB incidences in 2018 were male [2]. Other studies done in Ethiopia also showed > 50% of the notified TB cases to be males [16–17]. The M:F ratio for notification in the refugee camps was > 1.1:1 across the study period.

TB affects all age groups but disproportionally. According to 2018 WHO report, people in the age group 15–24 years in the globe and 15–34 years in Ethiopia are disproportionately affected by TB [2]. Similarly, in the refugee camps in Ethiopia, TB patients in the age groups 15–44 years represented 52.5% of the notified TB cases. Therefore, as people in this age group represents an active component of the workforce and have major impact on the socioeconomic of the society, the refugee TB programs and partners should tailor interventions and case finding efforts focusing on the age group 15 to 44 years.

Pediatric TB can has been considered as a sentinel for TB transmission. The contribution of children (< 15 years) to total TB cases notified in the refugee camps was increased from 18.8% in 2014 to 30.1% in 2017. Moreover, the contribution of children to total EPTB was also highest across the years and increased from 40.6% in 2014 to 65.1% in 2017. Globally, 10% of the TB incidence in 2018 were children (aged < 15 years) [2]. Although need further investigation, the increase in childhood TB could be due to real increase in TB transmission and incidence, an increase in number of children among refugees, and introduction of improved diagnostics like Gene Xpert. Thus, reaching missed adult TB cases, nutritional support, identification and management of child hood TB, and increasing BCG immunization coverage is recommended in the refugee camps.

HIV co-morbidity is one of the most important risk factors for TB. ART on the other hand plays significant role in reducing TB related morbidity and mortally, and TB incidence [18]. Across the study period, highest HIV prevalence (13.9%-21.6%) among the TB patient was observed in Gambella, followed by Shire and Jijiga areas. Previous study conducted in Gambella also showed 31.2% HIV co-infection among refugee TB patients [15]. Among the HIV positive TB patients in the refugee camps, 84.2% were on ART in 2017. This is low as compared to the 92% HIV positive TB patients in Ethiopia who were on ART [2]. These evidences suggest the need to strengthen the TB/HIV collaborative activities in the refugee camps with special focus to Gambella, Shire and Jijiga refugee areas.

The priorities of a TB programme are to identify and treat infectious TB patients with smear-positive PTB and those with severe forms of the disease. Thus, cure of infectious patients is the most effective means of reducing TB transmission in the family and community. In the refugee camps, cure rate for all TB cases was increased from 18.8% in 2014 to 27.7% in 2017. However, the average 24.7% cure rate in the refugee camps was lower than the 28.5% cure rate for TB patients registered in 722 districts for the period 2015–2017 in Ethiopia, and extremely lower than the 85% threshold suggested by WHO [19]. This lower cure rate can be improved by taking measures to improve follow-up sputum smear and culture examination, recording and reporting system, refresher training to health professionals, and engagement of patients, care givers and communities. Moreover, the average 50.4% treatment completed rate for TB patients in the refugee camps (either follow up sputum smear is not done or results are not recorded) was lower than the 62.4% treatment completed rate for TB patients registered in 722 districts for the period 2015–2017 in Ethiopia [19]. The results indicate the gap in performing follow up sputum smear examination, patient monitoring and in recording and reporting system in the refugee camps which need interventional actions.

According to WHO 90-(90)-90 global targets (which should be reached ideally by 2020 and at the latest by 2025), at least 90% treatment success rate need to be achieved among people on TB treatment in order to end TB by 2035 [2]. In this study, despite the increased trend in the number of notified TB cases, treatment success rate from 2014 to 2017 remained lower and stable at 72.4–79.4% for all TB cases and 72.5–

80.1% for new and relapse TB cases. This is lower than the 90% global target [2], 85% global and 96.0% national (Ethiopia) treatment success rate for new and relapse cases in 2017 [2], and the 94% treatment success for bacteriologically confirmed PTB cases in Ethiopia [13]. However, the mean treatment success rate in the refugee camps (75.1%) was higher than that reported in refugee camps in Syrian (63.6%) [20], in Gambella, Ethiopia (74.2%) [17], and other refugee camps in different part of the world (66.5–77.5%) [21–24].

The stable and lower treatment success rate in Ethiopia refugee camps was attributed to higher "not evaluated" (8.5%-13.1%), LTFU (5.6%-8.9%), and Died (3.6%-5.4%) treatment outcomes. Other studies conducted in Ethiopia showed 8.5%-18.3% LTFU rates [17, 25, 26] and 0.2%-7.8% treatment failure [17, 27]. Interestingly, of the sputum smear positive cases in 2017, 16 (20.3%) were not registered in the Lab and Unit TB register *(LTFU before treatment).* This could have significant negative impact on the clinical outcome of the patients as well as on TB transmission.

Together, the lower treatment success rate, the gaps in LTFU, death, not evaluated outcomes, and LTFU before treatment in the refugee camps can be addressed by improving TB recording and reporting system, refresher training, supportive supervision, regular monitoring and evaluation, improving diagnostic and treatment services, regular communication and collaboration between health professionals, patients and community mobilizers in defaulter tracing. However, further research is also warranted to identify other possible contributing factors for the low TB treatment outcomes in the refugee comes in order to achieve the global target (90%).

Understanding factors associated with unsuccessful treatment outcomes can help to design appropriate interventions. The multivariate logistic regression revealed that pretreatment weight < 40 kg, older age (> 45 years), and HIV infection independently associated with unsuccessful treatment outcomes. Independent association of older age (> 30 years [28], retreatment and HIV co-infected [26] with unfavorable treatment outcome was also reported by others. Thus, TB patients with pretreatment weight < 40 kg, older age (> 45 years), and HIV infected need special social and economic support, early diagnosis and close monitoring throughout their treatment period in the refugee camps in Ethiopia.

The positive association of the age group > 45 years with unsuccessful treatment outcome could be that this age group have a higher tendency not to adhere to anti-TB treatment because of tightness with work, travel a long distance to search work and addicted to alcohol [29]. The positive association of HIV infection with unsuccessful treatment outcome could be due less adherence of HIV patients to TB treatment due to drug burden or it could be due to less drug absorption related to due to drug-drug interaction.

Our analysis has some limitations. First, since this study was conducted retrospectively using secondary data, data quality could be an issue. Thus, some important socioeconomic and clinical data of the TB patients could be missed (not documented, lost, or TB register not contain information). However, maximum effort has been done to maintain the data quality standards including training of data collectors and supervisors, daily supervision, 10% data re-entry at the field, and data verification during data entry and analysis. Secondly, the use of secondary data in this retrospective study did not permit an analysis of patient socioeconomic and health facility level factors that may be associated with unsuccessful treatment outcomes. Third, analysis of MDR-TB was not included because a data collection system for DR-TB has not been fully established in the refugee camps.

The strengths of the study

despite these limitations, we have provided useful information on the performance of TB program in seven refugee areas over four year timespan in Ethiopia that will help to guide future TB control efforts in refugee camps.

5. Conclusions

This study provided useful evidence which will help to improve the effectiveness of TB programs in the refugee camps. The number of notified TB cases of all forms, and the proportion of EPTB and bacteriologically confirmed pulmonary new and relapse cases was increased from 2014 to 2017. The contribution of children (< 15 years) to the total notified TB cases of all forms and to EPTB has increased from 2014 to 2017. Men and age groups 15–44 represented the highest proportion of the notified TB cases during the study period. TB treatment success rate remained far lower below the global target (90%) and needs to be improved. The higher proportion of LTFU and “not evaluated” outcomes can be improved by intensifying patient monitoring and follow-up. Special socioeconomic support and close monitoring is recommended for TB patients who are at risk for unsuccessful treatment (pretreatment weight < 40 kg, > 45 years, and HIV infected). TB programs in the refugee camps should actively focus on TB prevention and routine screening targeting women, children, and age groups 15–44. Overall, our data indicated the need to strengthen TB recording and reporting system, supportive supervision, regular monitoring, continuous refresher training to health professionals, and collaboration among health care providers in the refugee camps.

Abbreviations

aOR
adjusted odds ratio; ART:Antiretroviral treatment; ARRA:Agency for refugee and returnee Affair; CNR:case notification rate; DP:displaced populations; EPTB:Extrapulmonary PTB; HIV:Human Immunodeficiency virus; LTFU:lost-to-follow up; MDR:multi-drug resistant; MTB:Mycobacterium tuberculosis; PTB:pulmonary TB; PTB+:smear positive pulmonary TB; P/Neg:smear negative pulmonary TB; RIF:Rifampicin; TB:Tuberculosis; WHO:world health organization

Declarations

Ethics approval and consent to participate

Ethical approval was obtained from Federal Ministry of Health, as well as from Agency for refugee and returnee Affair (ARRA), Ethiopia. A detailed explanation of the objective of the study was given to the managers of the refugee health facilities and permission was obtained to conduct the study. Patient registration number were used to maintain the study participant's confidentiality.

Consent for publication

Not applicable

Availability of data and materials

All data generated or analysed during this study are included in this published article

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

TL, GA, DK Kassa and DK Kebede designed the research. SG, EW, BF, YT, AB, BD, YD, HM, KA, and AA participated in data collection. TL and DK Kassa analyzed the data and develop the manuscript with input from all authors. All authors read and approved the final manuscript.

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30. Supplement. **1**: **Distribution of the notified TB case in the seven refugee areas and 25 refugee health facilities/camps in Ethiopia** (**2014**–**2017**).

Figures

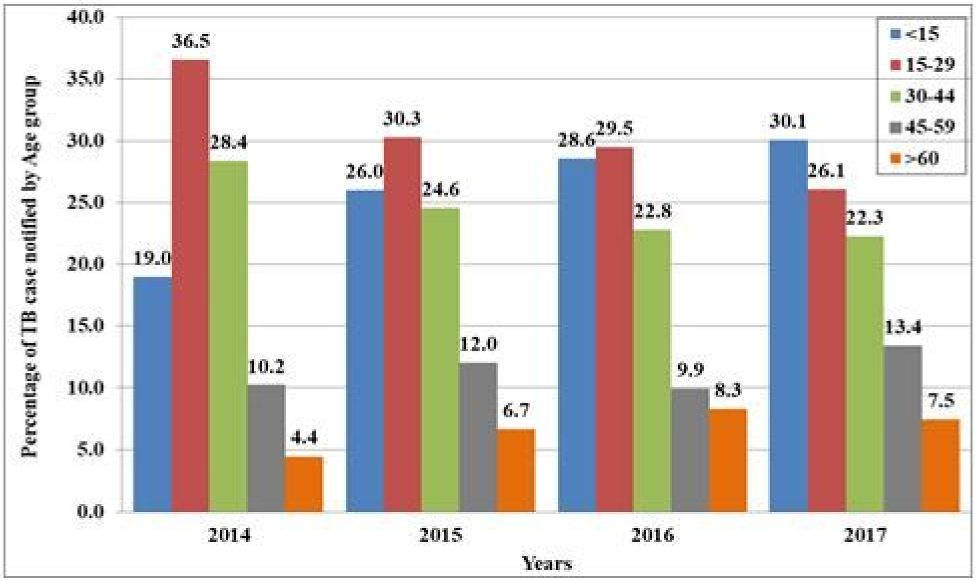

Figure 1

Total TB case notified in the refugee camps in Ethiopia disaggregated by age category, 2014 to 2017

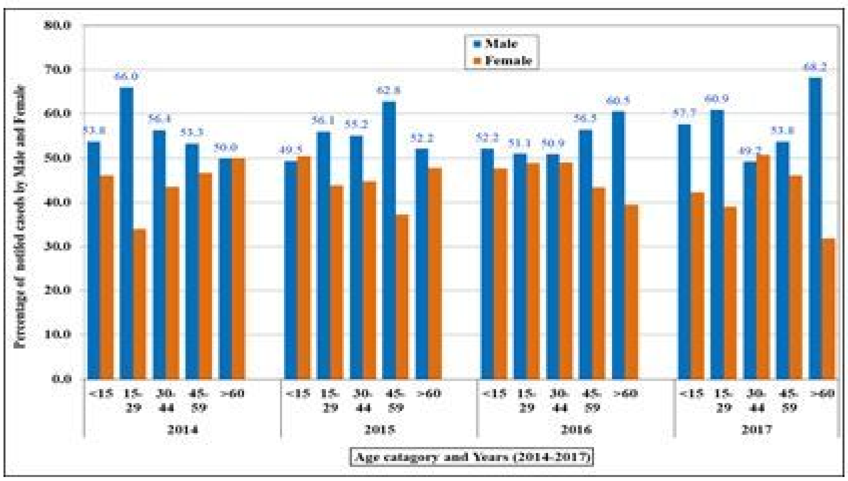

Figure 2

TB cases notified in the refugee camps in Ethiopia by age group and sex, 2014 to 2017.

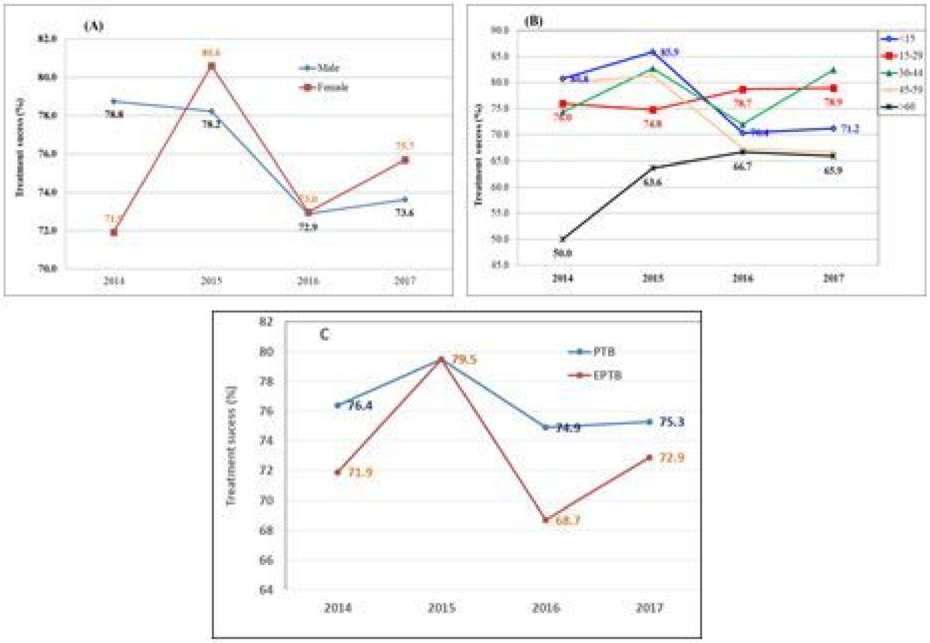

Figure 3

TB treatment success rate of the TB cases registered in the refugee camps in Ethiopia by gender (A), age category (B), and by type of TB (C).