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Original Article

Incidence and Factors Associated with Default Among Adults Treated for Tuberculosis in Two Regions of Cameroon

Incidence et facteurs associés aux perdus de vue chez les adultes traités pour tuberculose dans deux régions du Cameroun

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ABSTRACT

Introduction. Tuberculosis (TB) remains a public health problem worldwide. Our purpose was to determine the incidence and predictors of lost to follow up (LTFU) in TB patients. **Methods.** A retrospective study of adults treated for TB from 2010 to 2015 was carried out in all Diagnosis and Treatment Centres in West and North regions of Cameroon. Data was obtained from registers. Logistic regression was used to determine independent factors associated to LTFU. **Results.** Of the 19277 patients included, 12293 (63.8%) subjects were male and the median age (25^{th}-75^{th} percentile) was 34 (26-45) years. The incidence (95% CI) of LTFU was 2.9% (2.7-3.1%). The independent associated factors [Odds Ratio (95% CI)] with LTFU among patients treated for TB were: age ≤34 years [1.569(1.243-1.980), p<0.001], male gender [2.003(1.532-2.618), p<0.001], weight <50^{th} percentile [1.609(1.273-2.035), p<0.001], smear positive pulmonary TB (SPPTB) [2.179(1.252-3.792), p=0.006], patients previously treated [2.958(1.981-4.417), p<0.001] and unknown HIV status [2.847(2.102-3.856), p<0.001]. **Conclusion.** The incidence of LTFU among adults treated for TB is relatively low in West and North regions of Cameroon. Age ≤ 34 years, male sex, low weight, SPPTB, retreatment and unknown HIV status are its independent associated factors. TB patients on treatment presenting these factors should be closely monitored.

RÉSUMÉ

Introduction. La tuberculose (TB) reste un réel problème de santé publique mondial. Le but de notre étude était de déterminer l'incidence et les facteurs prédictifs des perdus de vue (PDV) au cours du traitement de la tuberculose. **Méthodes :** Une étude rétrospective incluant les adultes traités pour TB de 2010 à 2015 a été réalisée dans les Centres de Diagnostic et de Traitement de la TB dans les régions de l'Ouest et du Nord au Cameroun. Les données étaient extraites des registres. La régression logistique a été utilisée pour déterminer les facteurs indépendants associés aux PDV. **Résultats.** Des 19277 patients inclus, 12293 (63,8%) sujets était de sexe masculin et leur âge médian (25^{e}-75^{e} percentile) était de 34(26-45) ans. L'incidence (IC à 95%) de PDV était de 2,9% (2,7-3,1%). Les facteurs indépendant associés [Odds Ratio (IC à 95%)] de PDV au cours du traitement de la TB étaient : l'âge ≤34 ans [1,569(1,243-1,980), p<0,001], le sexe masculin [2,003(1,532-2,618), p<0,001], le poids < médiane [1,609(1,273-2.,035), p<0,001], la TB pulmonaire à microscopie positive (TPM+) [2,179(1,252-3,792), p=0,006], les patients retraités [2,958(1,981-4,417), p<0,001] et le statut VIH inconnu [2,847(2,102-3,856), p<0,001]. **Conclusion :** L'incidence de PDV au cours du traitement de la TB reste relativement faible dans les régions de l'Ouest et du Nord. Les facteurs prédictifs de PDV sont : âge ≤ 34 ans, sexe masculin, poids, TPM+, retraitement et statut VIH inconnu. Les patients présentant ces facteurs de risque, devraient être étroitement suivi au cours du traitement de la TB.

INTRODUCTION

Introduction

Tuberculosis (TB) remains a major public health problem worldwide. It is one of the top ten infectious disease causes of death globally according to the World Health Organization (WHO). To end TB, WHO proposes to reduce the number of deaths by 95% and its incidence by 90% from 2015 to 2035 [1]. Hence, one of the most important element in TB control is to ensure that each patient successfully finishes a complete course of treatment [1,2]. Loss to follow up (LTFU) defined by the WHO as discontinuation of TB treatment for at least two consecutive months after having taken TB treatment for one month is one of the causes of an incomplete course of treatment [3]. An incomplete course of treatment can

prevent patients from dying but this can have serious deleterious effects from the public health perspective. If the patients survive for prolonged periods of time while still harbouring the TB bacilli, this can result in prolonged periods of infectiousness, spread of disease and development of resistance to anti-TB drugs and ultimately deaths [4].

In Cameroon TB remains a common disease with an estimated incidence rate of 186 per 100,000 population [2]. Considerable efforts have been made in TB control in the country with the implementation of a network of Diagnostic and Treatment Centres (DTCs) over the entire national territory [5]. However, despite these efforts, TB control is still heavily hampered by among other things, difficult socioeconomic conditions, HIV infection and possibly LTFU of patients under treatment for TB. Indeed in a study conducted in Yaounde, it was observed that the rates of LTFU were quite high being at 20.0% in 2009 [4] and 37.9% in 2016 [6]. Another Cameroonian study in 2017 conducted in Douala, found a high rate of LTFU at 23.1% [7]. The rates of LTFU were high in those two biggest towns, but little was known in other regions of Cameroon. The present study was undertaken to determine incidence and factors associated with LTFU in patients treated for tuberculosis in two regions of Cameroon.

MATERIALS AND METHODS

Design and study population

The study population consisted of a retrospective cohort of all TB patients aged 15 years and more who were put on TB treatment in all the TB DTCs of the West and North regions between January 2010 and December 2015 (duration 5 years). Patients were included in the study if they were aged 15 years or more and presented with an incident case of TB. Patients with incomplete records, those lost to follow-up prior to commencement of treatment, as well as those transferred to DTCs out of the two regions of the study and those who were diagnosed with rifampicin or multidrug resistant TB were excluded.

Study setting

The study was conducted in all the TB Diagnostic and Treatment Centres (DTCs) in two regions of Cameroon, namely the West and North regions. During the study period, there were 20 functional TB DTC in West region and 17 functional TB DTC in North Region. In these centres and in accordance with the guidelines of the National TB Control Programme (NTCP), TB can be diagnosed as smear positive pulmonary TB (SPPTB), smear negative pulmonary TB (SNPTB) or extrapulmonary TB (EPTB) [3]. All patients diagnosed with TB are further classified as new or previously treated cases (relapse, treatment failure, and return after default). The diagnosis, treatment and follow-up of TB cases was described in our previous study [4]. All new cases are treated with a category 1 regimen for 6 months. It consists of the daily administration of rifampicin (R), isoniazid (H), ethambutol (E), and pyrazinamide (Z) for the first two months (intensive phase) followed by four months of rifampicin and isoniazid (2RHEZ/4RH). Previously treated patients undergo a category II treatment regimen for a total duration of 8 months. It consists of the daily administration of 2RHEZS/1RHEZ/5RHE. Antituberculosis drugs and antiretroviral therapy are given free of charge.

The outcomes of patients at the end of treatment are recorded into one of the following six mutually exclusive categories according to recommendations of the WHO and NTCP [3]: 1) Cured: treatment completed with a negative sputum smear in the last month of treatment and on at least one previous occasion; 2) Treatment completed: patient who has completed treatment but does not meet the criteria to be classified as cure or failure; 3) Treatment failure: patient who is sputum smear positive at 5 months or later during treatment; 4) Died: patient who dies for any reason during the course of treatment; 5) Lost to follow-up: patient whose treatment is interrupted for two consecutive months or more; 6) Transferred out: patient who has been transferred to another recording and reporting unit for whom treatment outcome is unknown.

Data collection

All TB patients enrolled on treatment during the study period in all the DTCs of the West and North regions were identified through a review of the TB registers and patients' treatment forms. Data extracted for each patient were recorded on a pre-prepared electronic data collection form developed in Epidata version 3.1 (Epidata Association, Lauritzen, Denmark). For each patient identified, the following information was extracted: name and region of DTC, age, gender, and place of treatment. The clinical baseline data were: weight, type of TB (new cases or previously treated case), form of TB (SPPTB, SNPTB, EPTB) and HIV status. Information was equally extracted and recorded for each patient on the following: sputum smear results at baseline and at the end of 2nd or 3rd, 5th and 6th or 8th month of treatment, as well as treatment outcomes. A patient was considered as having a successful treatment outcome if he/she was cured or had completed treatment.

Data analysis

Data analysis was performed using version 23 Statistical Package for Social Science (SPSS) software for Windows (SPSS Inc., Chicago, IL). Qualitative variables were represented in the form of proportion. Continuous variables were expressed by their average [standard deviation (SD)] when the distribution was normal or they were represented by their median (25th-75th percentiles). The incidence of LTFU was calculated as the proportion of default patients plus its 95% confidence interval (CI). Chi-square was used to compare proportions while the student t-test or Mann Whithney when appropriate was used to compare means. Multinominal logistic regression analysis was performed using variables found to be significantly associated with LTFU in the bivariate analysis to identify those that were independently associated with it. A p-value < 0.05 was used to characterize significant results.

Ethical issues

For retrospective studies there is no obligation for ethics approval. Nevertheless, administrative authorization to

conduct the study in the DTCs was obtained from the authorities of the Regional Delegations of Public Health.

RESULTS

During the study period 19958 TB patients were enrolled on antituberculosis treatment in all the DTCs of the two regions studied. Of these 404 (2.02%) were excluded because they were transferred out from the DTCs of the two regions to centres in other regions where they continued with their treatment. Another 277 (1.4%) of these patients were excluded from the study because of incomplete records.

General characteristics of the study population

Of the 19277 patients included in the study, males made up the majority with a total of 12293 (63.8) subjects. The median age (25^{th}-75^{th} percentiles) was 34 (26-45) years. The general characteristics of the study population are represented on table I. Pulmonary TB was predominant in 88.5% of cases. For EPTB localization, the pleura was the most affected site in 28.1% of cases, then lymph node in 20.3% and vertebrae in 11.1% of cases.

Table 1: General characteristics of the study population

Characteristics	N = 19277 (%)
Age, years	
Mean (SD)	37.1 (14.4)
Median (25^{th}-75^{th})	34 (26-45)
≤ 34	9650 (50.1)
> 34	9627 (49.9)
Minimum-Maximum	15-120
Gender	
Female	6984 (36.2)
Male	12293 (63.8)
Region of registration	
West	7706 (40.0)
North	11571 (60.0)
Year of registration	
2010	3132 (16.2)
2011	3244 (16.8)
2012	3288 (17.1)
2013	2997 (15.5)
2014	3202 (16.6)
2015	3414 (17.7)
Type of patients	
Previously treated	868/19101 (4.5)
New cases	18233/19101 (95.5)
Referred patients	
Yes	419/19267 (2.2)
No	18848/19267 (97.8)
Weight, kg	
Mean (SD)	56.6 (11)
Median (IQR)	56 (14)
< 25^{th} percentile	2005/8003 (25.1)
25^{th} - 50^{th} percentile	1907/8003 (23.8)
50^{th} - 75^{th} percentile	2115/8003 (26.4)
> 75^{th} percentile	1976/8003 (24.7)
Form of tuberculosis	
EPTB	2221 (11.5)
SNPTB	1827 (9.5)
SPPTB	15229 (79.0)
HIV status	
Positive	5029 (26.0)
Negative	12311 (64.0)
Unknown	1937 (10.0)

People living with HIV were 5029 (29.0%) patients among those who have done HIV serology and their median (IQR) CD4 count was 150 (222)/mm^3.

Outcomes of treatment and incidence of loss to follow up

The distribution of the different outcomes of antituberculosis treatment of the 19277 patients is presented in Table 2. Of the 19277 patients, 16930 (87.8%) had a successful treatment outcome. Five hundred and sixty of the 19277 subjects were LTFU giving a cumulative incidence of LTFU of 2.90 % (95% CI = 2.7-3.1%). There was a decrease of the cumulative incidence of LTFU from 3.7% in 2010 to 2.5% in 2015, p=0,025. The incidence of LTFU was higher in North region and remained around 2% between 2010 to 2015 in that region. The median (IQR) delay of LTFU was 3 (2) months.

Table 2: Outcomes of treatment of 19277 tuberculosis patients studied

Outcomes	Frequency n=19277	Percentage (%)
Cured	11505	59.7
Completed treatment	5425	28.1
Death	1565	8.1
Failure	222	1.2
Lost to follow up	560	2.9

Factors associated with lost to follow up among patients treated for tuberculosis in the West and North regions of Cameroon

The characteristics of TB patients with a successful treatment outcome and LTFU are summarized in table 3. Bivariate analysis revealed that LTFU was associated with patients aged ≤ 34 years (56.8% versus 51.2%, p=0.009). There was a decrease of proportion of defaulters in 2014 and 2015 compared to years before 2013 (p=0.001). Male patients were frequently LTFU compared to female patients (p<0.001). Reference was associated to LTFU (3.9% versus 2.2%, p=0.007). Patients previously treated (7.8% versus 4.3%, p<0.001) and SPPTB (94.6% versus 78.2%, p<0.001) were more likely to LTFU. HIV positive statistically reduced the proportion of patients LTFU among patients treated for TB (15.5% versus 23.2%, p=0.024), while unknow HIV status was an associated factor to LTFU (26.3% versus 9.7%, p<0.001).

After multivariate analysis (table 4), the independent determinants [odds ratio (95% CI)] with LTFU among patients treated for TB found in our study were: age ≤34 years [1.569(1.243-1.980), p<0.001], male gender [2.003(1.532-2.618), p<0.001], weight <50^{th} percentile [1.609(1.273-2.035), p<0.001], SPPTB [2.179(1.252-3.792), p=0.006], patients previously treated [2.958(1.981-4.417), p<0.001], unknown HIV status [2.847(2.102-3.856), p<0.001] and TB treatment in year 2012 [1.629(1.131-2.345), p=0.009].

Table 3: Comparison of baseline characteristics of patients with successful antituberculosis treatment outcome and those lost to follow-up during treatment

Characteristics	Univariate analysis		
	LTFU n =560 (%)	Sucessful outcome n = 16930 (%)	*p*
Age, median			
≤34 years	318 (56.8)	8668 (51.2)	0.009
>34 years	242 (43.2)	8262 (48.8)	
Gender			
Male	429 (76.6)	10760 (63.6)	<0.001
Female	131 (23.4)	6170 (36.4)	
Region of registration			
North	363 (64.8)	10740 (63.4)	0.503
West	197 (35.2)	6190 (36.6)	
Year of registration			
2010	116 (20.7)	2766 (15.7)	0.003
2011	92 (16.4)	2829 (16.7)	0.264
2012	109 (19.5)	2968 (16.9)	0.046
2013	97 (17.3)	2648 (15.6)	0.053
2014	62 (11.1)	2870 (18.1)	0.159
2015	84 (15.0)	3065 (18.1)	1
Referred patients			
Yes	22 (3.9)	372 (2.2)	0.007
No	538 (96.1)	16548 (97.8)	
Form of tuberculosis			
SPPTB	530 (94.6)	13235 (78.2)	<0.001
SNPTB	11 (2.0)	1777 (10.5)	0.1
EPTB	19 (3.4)	1918 (11.3)	1
Type of patients			
Previously treated	43 (7.8)	720 (4.3)	<0.001
New cases	511 (92.2)	16061 (95.7)	
Weight			
< 25th percentile	97 (29.2)	1504 (23.2)	<0.001
25^{th} - 50^{th} percentile	98 (29.5)	1530 (23.6)	0.002
50^{th} - 75^{th} percentile	82 (24.7)	1756 (27.1)	0.001
> 75^{th} percentile	55 (16.6)	1690 (26.1)	1
HIV status			
Positive	87 (15.5)	3978 (23.5)	0.024
Unknown	147 (26.3)	1637 (9.7)	<0.001
Negative	326 (58.2)	11315 (66.8)	1

LTFU: lost to follow up, SNPTB: smear negative pulmonary tuberculosis, SPPTB: smear positive pulmonary tuberculosis, EPTB: extra-pulmonary tuberculosis, HIV: human immunodeficiency virus

DISCUSSION

The objective of this study was to determine the incidence and factors associated to LTFU among patients treated for TB in two regions of Cameroon. At the end of our study, the incidence of LTFU was 2.9% in West and North regions of Cameroon. Independent associated factors with LTFU were: age, male gender, low weight, SPPTB, patients previously treated, unknow HIV status and TB treatment in 2012.

The incidence of patients LTFU found in our study was ranged between 2.6% to 4.0% as found in some developing countries [8–10]. A South African study found a higher rate of 7.0% defaulted patients [11]. Khalif et al in Somalia revealed 6.2% of defaulters [12]. An ethiopian study found a higher rate of 12.8% LTFU with only 42.7% of the cohort who had SPPTB, while 31% where SNPTB and 26.3% had EPTB [13]. This could be explain the fact that younger population (mean age of 32.4 years compared to 34 years in our study) doubt their TB diagnosis, and became defaulters. The LTFU outcome reached a rate of 20.0% in a previous study in the biggest referral center of the capital city of Cameroon, which was 10 times higher than the rate found in our cohort. Patients followed in the reference center in Yaounde, which having a large number of patients daily, increasing the waiting time would be favorable to LTFU. This could be also explained by the high rate of unknow HIV status of 14.3% compared to 10% in our cohort. Notice also that systematic effort was not put in place to trace defaulters. For instance, some patients who died during TB treatment would have been inappropriately classified as defaulters, particularly among HIV infected patients [14].

In Nigeria, the proportion of LTFU of 25.7%, in the city of Kano from 2010 to 2014 was approximatively ten times greater than the rate found in our cohort [15].

Table 4: Multivariate analysis of factors associated with loss to follow-up of treatment of TB patients from the West and North regions of Cameroon

Characteristics	OR (95% CI)	*p*
Age, median		
≤34 years	1.569 (1.243-1.980)	<0.001
>34 years	1	
Gender		
Male	2.003 (1.532-2.618)	<0.001
Female	1	
Year of registration		
2010	1.318 (0.880-1.973)	0.180
2011	1.312 (0.898-1.918)	0.161
2012	1.629 (1.131-2.345)	0.009
2013	1.291 (0.880-1.894)	0.191
2014	0.581 (0.360-0.936)	0.025
2015	1	
Referred patients		
Yes	1.885 (0.958-3.706)	0.066
No	1	
Form of tuberculosis		
SPPTB	2.179 (1.252-3.792)	0.006
SNPTB	0.841 (0.312-2.266)	0.732
EPTB	1	
Type of patients		
Previously treated	2.958 (1.981-4.417)	<0.001
New cases	1	
Weight		
≤ 50th percentile	1.609 (1.273-2.035)	<0.001
> 50th percentile	1	
HIV status		
Positive	0.800 (0.582-1.100)	0.169
Unknown	2.847 (2.102-3.856)	<0.001
Negative	1	

LTFU: lost to follow up, OR: Odds ratio, CI: confidence interval, SNPTB: smear negative pulmonary tuberculosis, SPPTB: smear positive pulmonary tuberculosis, EPTB: extra-pulmonary tuberculosis, HIV: human immunodeficiency virus

This could be explained by the high proportion of TB/HIV co-infection which was due to Boko Haram insurgency in Kano state where that study has be done, leading to a large number of displaced and vulnerable populations [15,16].

Young age was found to be a predictor of LTFU in some studies [17–19]. Their results are similar to those of our study, in which the median age was 34 years [18]. Studies found that the 15-24 age group was associated with LTFU [19,20]. Shargie et al revealed that people over the age of 25 were more likely to default [17]. This can be explained by behaviors of young people and their high physical functioning score which was a strong predictor of defaulters as revealed by a Nigerian study [21].

Some studies conducted in developing countries reported that male sex was a factor associated to defaulters, as found in our study [19,22,23]. Mulongeni et al determined that male gender was a factor for LTFU from TB care [20]. This difference between gender might be related by social, economic, biological, educational, behavioral and environmental factors which were not investigated in this study. Some studies revealed that patients without known HIV status had significantly higher default, as found in our study [4,24,25]. Those patients were more LTFU because they want to escape the pressure put on them by health workers for testing.

HIV was not a predictor of LTFU in our study due the to low rate of co-infection (15.5% in defaulters versus 23.5% in favorable outcome, p=0.024) as noticed in an ethiopian study with solely 12.4% HIV/TB co-infection [13]. In south Africa, having had prior treatment for TB were factors associated to LTFU, as found in our study [20,26]. SPPTB was an associated factor to LTFU, as revealed in an ethiopian study which were found that reasons of defaulting were lack of family support, inadequate knowledge about the duration and medication side effects [27]. Anti-tuberculosis treatment in 2012 was a predictor of LTFU while TB treatment after the year 2013, was a protective factor of LTFU. This can be explained by the fact that it was during this year 2013, that Cameroon adopted the strategy of antiretroviral therapy for all TB patients regardless of the CD4 level. Thus, the number of patients living with HIV was lower in DTCs, thus reducing the number of LTFU due to HIV.

The limitations of our study were essentially link to the retrospective nature of the design with data collection on DTC registers. This study fails to identify certain demographic, clinical, radiological and biological variables in order to determine other potentials predictors of lost to follow up during tuberculosis treatment. The large sample size of our study is a strong point for this retrospective cohort of TB patients.

CONCLUSION

The incidence of loss to follow-up in patients under TB treatment between 2010 and 2015 in the West and North regions of Cameroon was relatively low. Male gender, age ≤34 years, low weight, unknown HIV status, patients previously treated and SPPTB were independent factors associated with LTFU of patients under antituberculosis treatment in these two regions. As such TB patients presenting these factors should be closely monitored when on treatment in a bid to limit treatment default.

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CONFLICT OF INTEREST

The authors declared no conflict of interest.

CONTRIBUTIONS TO THE STUDY

ADB[a,b,c,d], VPM[a,c,d], AK[c,d], LMT[a,b], JTL[a,b], ADK[a,b], DMM[a,b], FDR[a,b], EWPY[a,b,c,d], CK[a,b,c,d]

[a] Design and development of the study

[b] Data analysis and interpretation

[c] Article writing or critical analysis that brings about significant changes

[d] Final approval of the submitted version after critical review

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