Treatment outcome of tuberculosis patients with HIV under Directly Observed Treatment Short Course (DOTS) in Lubumbashi (D.R. Congo).

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Abstract

Introduction: Tuberculosis (TB) is one of the major public health and socio-economic issues in the 21st century globally. Assessment of TB treatment outcomes, and monitoring and evaluation of its risk factors in Directly Observed Treatment Short Course (DOTS) are among the major indicators of the performance of a national TB control program. Thus, the current study was carried to evaluate outcomes and to determine factors affecting outcome in TB patients with HIV.

Materials and Methods: Between January 2010 to December 2014 all tuberculosis patients enrolled in DOTS clinic of the Lubumbashi's Health Zone were collected retrospectively from the TB registration book. We compared the data for TB patients of HIV positive and negative subjects. Medical records of the patients were reviewed for age, gender, type, category and treatment outcome.

Results: A total of 3558 tuberculosis patients were registered in the Lubumbashi's Health Zone between January 2010-December 2014. Of these, 2063 (57.98%) were male, 1502 (42.02%) were smear positive pulmonary TB (PTB+), 125 (3.51%) were smear negative pulmonary TB (PTB-) and 1931(54.27%) were extra pulmonary TB (EPTB) patients. We evaluated 1653 registered patients (HIV screening rate: 46.46%), of these, 256(15.49%) were HIV positive patients. The overall treatment success rate was 83.3% and failure rate 16.7% of tuberculosis patients with and without HIV. Tuberculosis type, age, outcome and category of TB patients were significantly associated with TB-HIV co-infection. PTB+ patients and others category of patients were significantly adverse for outcome of patients with TB-HIV co-infection.

Conclusion: It appears that DOTS have improved treatment success in the Lubumbashi's Health Zone for five years. However, this study shows clearly that TB-HIV coinfection have a negatively impacts on TB treatment outcome and TB screening should be encouraged in TB patients.

Keywords: Tuberculosis, Opportunistic infection, Human immunodeficiency virus, Chronic infectious diseases, HIV-TB co-infection

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Introduction

Despite the avaibility of effective drugs, tuberculosis (TB) is still a global emergency and one of the major public health problems in the 21th century [1]. It is not only a public health problem, but also a socio-economic issue [2].

According to the 2014 report of World Health Organization (WHO), there were 9.6 million new TB cases and 1.5 million deaths from TB worldwide [3]. The 30 high TB burden countries collectively account for 85-89% of the global burden. Democratic Republic of the Congo (DRC) is among the 30 high burden country for TB [4] in the world with an estimated TB incidence of 323 per 1,00,000 population in 2016. The mortality of all forms of TB in DRC was estimated to be 67 per 1,00,000 population [5].

TB is the commonest opportunistic infection and leading cause of death in human immunodeficiency virus (HIV) patients in developing countries and account for about 40% of all manifestations seen in HIV patients [6]. The intricate linkage of TB and HIV infection for nearly the past 3 decades poses a major threat to the international community's effort to achieve the health-related United Nations Millennium Development Goal for TB and HIV infection [7]. TB-HIV co-infection is the strongest known risk factor for progression for latent TB infection to TB disease [8].

The Directly Observed Treatment Short Course (DOTS) strategy, which allows patients to take their daily drugs under the observation of health professionals, thereby improving treatment compliance, has been known to increase TB cure rate. In DRC, several strategies have been put in place to combat this

disease; DOTS in 1996, which, in 1999, became the Stop TB strategy [9].

Treatment outcome is an important indicator of TB control programs [10] and monitoring and evaluation of treatment outcome of TB patients is an integral part of the DOTS strategy [11]. Despite the high TB burden and DOTS coverage in the study zone however, no study has so far assessed trends of TB case notifications, treatment success rate at a larger scale. Thus, the current study was carried to evaluate outcomes and to determine factors affecting outcome in TB patients with HIV.

Methods

Study design and setting

We conducted a retrospective cohort study from January 2010 to December 2014 in the Lubumbashi's Health Zone, one of the 27 Health Zones of Haut-Katanga's Province in the South of the Democratic Republic of Congo. It has 3 Directly Observed Treatment Short-Course Clinics: University Teaching Hospital of Lubumbashi, Jason Sendwe Provincial Referral Hospital, Centre Médical du Centre-Ville (CMDC).

Participants

Patients included in the study were subjects of any age diagnosed with TB and consecutively recorded in the registry of each clinical.

Data collection

Basic demographic data such patient's age, gender, HIV sero-status, TB patient category, and type of TB and treatment outcome were included in the collecting format.

Operational definition

According to the standard definitions of the National TB and Leprosy Control Program (NTLCP) of DRC adopted from WHO [9], the following clinical case, types of TB and treatment outcome operational terms were used:

- Smear-positive pulmonary TB (PTB+): A patient with at least two sputum specimens which were positive for acid fast bacilli (AFB) by microscopy, or a patient with only one sputum specimen which was positive for AFB by microscopy, and chest radiographic abnormalities consistent with active PTB.
- Smear-negative pulmonary TB (PTB-): A patient with symptoms suggestive of TB, with at least two sputum specimens which were negative for AFB by microscopy, and with chest radiographic abnormalities consistent with active PTB, or a patient with two sets of at least two sputum specimens taken at least two weeks apart, and which were negative for AFB by microscopy, and radiographic abnormalities consistent with PTB and lack of clinical response to one week of broad spectrum antibiotic therapy.
- Extra pulmonary TB (EPTB): This included TB of organs other than the lungs, such as lymph nodes, abdomen, genitourinary tract, skin, joints and bones, the meninges and others. Diagnosis of EPTB was based on fine needle aspiration cytology or biochemical analyses of cerebrospinal/pleural/ascitic fluid or histopathological examination or strong clinical evidence consistent with active EPTB, followed by a decision of a clinician to treat with a full course of anti-TB chemotherapy. In all the cases of EPTB, sputum examinations and chest radiographs were used to rule out involvement of the lung parenchyma. This hospital lacks the facilities for culture and drug susceptibility testing.
- Successful outcome: If TB patients were cured (negative smear microscopy at the end of treatment and on at least one previous follow-up test) or completed treatment with resolution of symptoms.
- Unsuccessful outcome: If treatment resulted in treatment failure (remaining smear-positive after 5 months of treatment), defaulted (patients who interrupted their treatment for two consecutive months or more after registration), or died.

Statistical analysis

Data were entered, cleaned and analyzed using SPSS for windows, version 20. Proportions with 95% confidence intervals, Odds ratio and Chi-square tests were employed to compare diverse groups for categorical data. P-value <0.05 were considered statistically significant.

Ethical statement

The study was authorized by the ethics committee of the University of Lubumbashi and the Health authority of Haut-Katanga Province before data collection. Patient records/ information was anonymized and de-identified prior to analysis to ensure confidentiality of individual patient information.

Results

Table 1 shows that most registered patients are male (57.98%) and the most affected are group is under 30 years of age. In Table 2, we find that the nearly half of TB patients had EPTB (54.27%), 90.05% of these patients were new cases. Regarding TB-HIV co-infection, a screening rate of 46.46% was obtained and a HIV seroprevalence of 15.5% was found. Table 3 shows an average incidence of 447 TB case notifications per 100,000 population during this study period.

Table 4 shows successful treatment rate of 83.3% in general and the mortality rate in all TB patients was 7.39%. Table 5 shows that TB-HIV co-infection was significantly associated within age, type of TB, outcome and patient category. The TB-HIV co-infection rate was significantly higher in patients over 40 years of age, in those with PTB- and EPTB, in those with an adverse course, and in those who had already been treated with anti-TB drugs. Regarding the outcome of HIV infected TB patients (Table 6), it was significantly unfavorable in those with PTB+ (OR=1.93 [1.03-3.64]) and in previously treated patient anti-TB drugs (OR=2.59 [1.18-5.66]).

Discussion

TB is one of the chronic infectious diseases, which remained a significant cause of morbidity and mortality for poor nations.

Table 1. *Socio-demographics characteristics (age, sex) of the registered TB cases (n=3558).*

TB Type	Sex		Age (years)				Total (%)
	Male	Female	< 30	30-39	40-49	≥ 50	
PTB+	911 (44.16%)	591 (39.53%)	717 (52.57%)	428 (41.51%)	202 (33.72%)	155 (27.48%)	1502 (42.02%)
PTB-	76 (3.68%)	49 (3.28%)	29 (2.13%)	34 (3.30%)	38 (6.34%)	24 (4.26%)	125 (3.51%)
EPTB	1076 (52.16%)	855 (57.19%)	618 (45.31%)	569 (55.19%)	359 (59.93%)	385 (68.26%)	1931 (54.27%)
All TB Cases	2063 (57.98%)	1495 (42.02%)	1364 (38.33%)	1031 (28.97%)	599 (16.84%)	564 (15.85%)	3558 (100%)

Table 2. *TB patient category and HIV status of the registered TB cases (n=3558).*

TB Type	HIV serology			TB patient category					Total (%)
	Positive	Negative	Unknown	New	Transfer in	Relapse	Interruption	Treatment failure	
PTB+	72 (28.13%)	634 (45.38%)	796 (41.78%)	1320 (41.20%)	43 (57.33%)	77 (77.00%)	40 (26.32%)	22 (81.48%)	1502 (42.02%)
PTB-	38 (14.84%)	50 (3.58%)	37 (1.94%)	102 (3.18%)	4 (5.34%)	3 (3.00%)	16 (10.53%)	0 (0.00%)	125 (3.51%)
EPTB	146 (57.03%)	713 (51.04%)	1072 (56.27%)	1782 (55.62%)	28 (37.33%)	20 (20.00%)	96 (63.16%)	5 (18.52%)	1931 (54.27%)
All TB Cases	256 (100%)	1397 (100%)	1905 (100%)	3204 (100%)	75 (100%)	100 (100%)	152 (100%)	27 (100%)	3558 (100%)

Table 3. *Trends of new TB case notifications.*

Treatment outcome	New case TB notified	Zonal population	TB case notification per 100,000 population per year
2010	626	134,809	464
2011	620	138,852	446
2012	578	143,018	404
2013	674	147,309	457
2014	706	151,728	465

Table 4. *Trends of treatment outcome of all forms registered TB cases (n=3558).*

Treatment outcome	2010	2011	2012	2013	2014	Total (%)
Cured	200 (27.17%)	211 (29.72%)	215 (33.91%)	245 (34.27%)	291 (38.14%)	1162 (32.66%)
Completed	398 (54.08%)	344 (48.45%)	306 (48.26%)	386 (53.99%)	369 (48.36%)	1803 (50.67%)
Total of successful treatment	598 (81.25%)	555 (78.17%)	521 (82.17%)	631 (88.25%)	660 (86.50%)	2965 (83.33%)
Default	24 (3.26%)	44 (6.20%)	22 (3.47%)	27 (3.78%)	26 (3.41%)	143 (4.02%)
Death	88 (11.96%)	51 (7.18%)	42 (6.62%)	38 (5.31%)	44 (5.77%)	263 (7.39%)
Transfer out	11 (1.49%)	18 (2.54%)	10 (1.58%)	6 (0.84%)	6 (0.79%)	51 (1.43%)
Failure	15 (2.04%)	42 (5.92%)	39 (6.15%)	13 (1.82%)	27 (3.54%)	136 (3.82%)
Total of unsuccessful treatment	138 (18.75%)	155 (21.73%)	113 (18.83%)	84 (11.75%)	103 (13.50%)	593 (16.67%)

Recently aggravated by the HIV epidemic, this remains a major public health problem in developing countries [12].

In this retrospective study, complete information was extracted from TB registration documents for a total of 3558 registered TB patients in five years. Most of the patients were male (57.98%) and similar results were seen in study by Ngama et al. in Lubumbashi [13], Cheru et al. in Gondar [6], Gebrezgabiher et al. in Southern Ethiopa [14] in contrast to previous studies done in Gambella [15]. The reason for male predominance is not well known. However, differences in men's and women's societal roles have an influence on their risk of exposure TB and case access to care. Women usually have reduced access to health care facilities in developing country [13,16].

In this study, 84.14% of registered TB patients fall in the range less than 50 years, the most productive age group. This range includes the most socio-economically productive members of the society who can, thus, pose challenges to the social and economic development of the community in the area and nation at large.

In the present study, EPTB was the prevailing form of TB (54,27%). Similar results was found by Ejeta et al. in Ethiopa [17] alors que Mbatchou et al. au Cameroun [16] et Dangisso et al. in Ethiopa considers that the PTB form remains the

Table 5. *Characteristics of study population in relation to HIV status (n=1653).*

Variables	HIV Status		Total (N=1653)	OR [CI 95%]	p-value
	HIV positive (n=256)	HIV negative (n=1397)			
Age (years)					
≤ 40	167 (13.94%)	1031 (86.06%)	1198 (100%)	1.00	
>40	89 (19.56%)	366 (80.44%)	455 (100%)	1.50 [1.13-1.99]	0.0060
Sex					
Male	138 (14.07%)	843 (60.34%)	981 (100%)	1.00	
Female	118 (17.56%)	554 (39.66%)	672 (100%)	1.30 [0.99-1.70]	0.0630
TB type					
PTB+	72 (10.20%)	634 (89.80%)	706 (100%)	1.00	
PTB-	38 (43.18%)	50 (56.82%)	88 (100%)	6.69 [4.11-10.89]	0.0000
EPTB	146 (17.00%)	713 (83.00%)	859 (100%)	1.80 [1.33-2.44]	0.0001
Outcome					
Success	194 (14.31%)	1162 (85.69%)	1356 (100%)	1.00	
Unsuccess	62 (20.88%)	235 (79.12%)	297 (100%)	1.58 [1.15-2.17]	0.0060
TB Patient Category					
New cases	225 (14.57%)	1319 (85.43%)	1544 (100%)	1.00	
Others	31 (28.44%)	78 (71.56%)	109 (100%)	2.32 [1.50-3.61]	0.0001

Table 6. *Factors affecting outcome in TB patients with HIV (n=256).*

Variables	Outcome		Total (N=256)	OR [CI 95%]	p-value
	Success treatment (n=194)	Unsuccess treatment (n=62)			
Age (years)					
≤ 40	123 (73.65%)	44 (26.35%)	167 (100%)	1.41 [0.75-2.62]	0.3493
>40	71 (79.78%)	18 (20.22%)	89 (100%)	1.00	
Sex					
Male	107 (77.54%)	31 (22.46%)	138 (100%)	1.00	
Female	87 (73.73%)	31 (26.27%)	118 (100%)	1.23 [0.69-2.18]	0.5737
TB type					
PTB+	48 (66.67%)	24 (33.33%)	72 (100%)	1.93 [1.03-3.64]	
PTB-	30 (78.95%)	8 (21.05%)	38 (100%)	1.03 [0.43-2.47]	0.0401
EPTB	116 (79.45%)	30 (20.55%)	146 (100%)	1.00	1.000
TB Patient Category					
New cases	176 (78.22%)	49 (21.78%)	225 (100%)	1.00	
Others	18 (58.06%)	13 (41.94%)	31 (100%)	2.59 [1.18-5.66]	0.0255

most important [18]. This difference could be explained by differences in medical practices related to the diagnostic criteria in our country and by the viability of a good technical platform for the confirmation of EPTB diagnosis.

The HIV testing rate found, in our study, was 46.46%. This rate did not meet the 85% WHO target [3]. This finding is probably due either to a high rate of refusal of HIV testing among TB patients, to a lower prescription of HIV testing by physicians or by the multiple break in HIV testing. The rate of HIV-TB co-infection in this study was 15.5% and this rate was lower than the results obtained in Nigeria [7,19].

Our study showed an overall treatment success of 83.3% which was slightly lower than the WHO treatment success report for DRC and the WHO target (85%) [20]. This performance might be due to improved adherence of TB patients to treatment that signify the importance of DOTS strategy.

In this series, some factors were related to TB-HIV co-infection such age less than 40 years, success outcome and old TB patients. This result reflects the poorer TB treatment outcomes in HIV positive individuals and this finding is similar to that of several other studies [7,21].

To determine factors affecting outcome in HIV-TB co-infection, we analyzed demographic and clinical determinants of treatment outcome. Our data showed that PTB+ patients and old patients were significantly adverse for outcome patients. Although in several studies, type of TB did not sign efficiently associated with unsuccessful treatment outcome [18,22], this finding highlights the need for alternative approaches to reduce morbidity and mortality resulting from this co-infection.

This study was associated with a few limitations. The missing data may have affected the results. The rate of types of TB (TB- , EPTB) may have been underestimated, as culture was not available, or these clinical forms of TB could also have been overestimated by physicians using clinical findings alone for diagnosis instead of biopsy.

Conclusion

In summary, this study shows that TB patient's treatment success rate of 83.3% in overall patients with HIV and without. It appears that DOTS have improved treatment success in the Lubumbashi's Health Zone. However, this shows clearly that HIV-TB co-infection have a negatively impacts to TB treatment outcome. So, TB screening should be encouraged in TB patients and ensuring high acceptance and early HIV screening in TB patients will contribute to improve the treatment success.

Authors Contributions

This work was carried out in collaboration between all authors. Authors CK, DN, HS and CM conceived and designed the study. Authors CK, PK, C Kibulungu and PM conducted and collected data. Authors CK, OM, MM, BT, DN, HS and CM contributed to data analysis, interpretation and manuscript review. Authors CK, OM, MM and BT wrote the manuscript. All authors read and approved the final manuscript.

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