Predictors of the occurrence of tuberculosis in HIV-infected adults during the first six months of antiretroviral therapy in Kisangani, DR Congo

ABSTRACTS

Objective: To determine the predictive factors for the occurrence of tuberculosis (TB) in adults infected with HIV during the first 6 months of antiretroviral therapy in Kisangani.

Methods: A case-control study was carried out during the period from January 1, 2017 to December 31, 2018. Clinical data were collected retrospectively from patients receiving antiretroviral therapy in the city of Kisangani. Out of a total of 1,161 HIV-infected patients included in this study, 58 of whom developed TB. Predictors of TB onset in these antiretroviral therapy patients were identified using logistic regression analysis.

Results: After multivariate analysis, the independent factors associated with the occurrence of TB were: being married (OR = 4.456; 95% CI: 1.061-18.713), residence in the municipality of Tshopo (OR = 7.04; 95% CI: 1.168-42.47) as well as stages 3 and 4 of AIDS disease (OR = 29 95% CI: 4.563-184.872 and OR = 50.8 95% CI: 3.971 -680.995).

Conclusion: The results found by this study highlight the need for active TB testing in HIV-infected individuals. Particular emphasis should be placed on the category of patients on antiretroviral therapy who have one of the independent factors for the onset of TB.

Keywords: Predictors, Tuberculosis, HIV, Antiretroviral Treatment, Kisangani.

Introduction

Tuberculosis (TB) is a real public health problem. In fact, it is estimated that approximately one third of the world population is infected with Mycobacterium tuberculosis. The advent of HIV / AIDS added to the unfavorable socio-demographic conditions of populations increases the vulnerability of this disease [1]. Thus, in Africa, it has been found to be common in the first six months of initiation of antiretroviral therapy (ART). TB occurring during this period is associated with high mortality [2, 3].

It is the most common opportunistic infection found in people living with HIV (PLHIV). [4] Globally, approximately 5-40% of patients enrolled in antiretroviral therapy services are diagnosed of TB [3].

In Africa, 10% of adults infected with HIV and started on ART die within the first year, with TB being the leading cause of death. (PECK, RN 2012) .Most studies across Africa on predictors of TB onset in adults infected with HIV during the first 6 months of initiating ART show that the factors independent at onset were: male, married subjects, alcohol consumption, presence of a TB patient in the family, BMI <18.5 and OMS4 clinical stages, low CD4 count, a low hemoglobin level when starting ART. The protective effect of isoniazid and cotrimozazole prophylaxis is also noted [1, 3, 4, 6,7].

Key interventions recommended to reduce the burden of TB in PLHIV include: scaling up TB testing and treatment, isoniazid preventive therapy, controlling TB infection and early onset of a ART [8].

However, to our knowledge, there is no study on the main factors favoring the occurrence of TB in PLWHA in DR Congo in general and in the city of Kisangani in particular.

It is in this context that the present study aims to determine the predictive factors for the occurrence of TB in adults infected with HIV during the first 6 months of initiating ART in Kisangani.

Population and Methods

This study was carried out in all general hospitals in the city of Kisangani. These hospitals were chosen because of their high attendance by PLHIV and the presence of medical staff trained in the management of HIV / AIDS. This was a case-control study during the period from January 1, 2017 to December 31, 2018. The cases are all PLHIV on ART and who have developed TB within the first 6 months of initiating ART, while the controls are PLHIV and who have not developed TB in the first 6 months of initiating ART.

In total, all of the PLWHA on ART made up the population of our study, i.e. 1,161 patients. Of these, 58 developed TB within the first 6 months of initiating ART. Cohort registers of patients on ART, PLHIV consultation cards, HIV and TB management cards were reviewed in order to collect the variables of interest, in this case age, sex, civil status, municipality of residence, date of the start of initiation of ART, clinical stages during the diagnosis of HIV disease, the result of BAAR research.

The data collected was grouped and presented through the percentage tables. The data were analyzed using SPSS version 20.0 and Microsoft Office Excel 2007. The data were expressed in the tables. We used percentage calculations, mean, Odd Ratio, nonparametric means comparison test, and univariate and multivariate logistic regression were performed to identify predictors of TB onset among PLHIV on ART. The statistical significance threshold used was set at 0.05 or 5%. The information collected from each PLWHIV file was completely confidential and remains forever disclosed.

They were used only for research purposes after obtaining the authorization of the health authorities of the province of Tshopo before carrying out this study.

Results

A number of factors have been studied for their potential association with the onset of TB in people on ART on ART within the first six months of initiating ART. Being married, living in Tshopo commune, AIDS stages 3 and 4 were the best predictors of the occurrence of TB in people on ART (see Table II) .Other predictors of TB on people on ART like men don't was not associated with the occurrence of TB during the multivariate analysis (see Table II). We did not find any information on CD4 count, viral load, hemoglobin level, BMI <18, 5, alcohol consumption, drug addiction, etc., which are also blamed elsewhere as factors associated with the onset of TB in PLWHA within the first six months of initiating ART [2,3,4 6.7].

Discussion

In our study, age was not associated with the onset of tuberculosis in PLWHA on ARVs (see Table I). This resembles the result of Panella et al. in Burkina Faso, in 2014, DANIEL W.G et al. in Tanzania, in 2018; PECK R. N et al. in Tanzania in 2012 where they found that age was not associated with the onset of tuberculosis [2,4,7].

Other shares ABGRALL et al. In France, in 1997-2008 had found that the age group varying between 15 and 46 years with an average of 39.7 ± 11.2 years was associated with the occurrence of TB at during the first six months of initiating ART. TB presents itself as a disease that mainly affects young adults. [9].

In our study, it turns out that male patients had an increased risk of developing TB (OR = 1.8 95% CI: 1.01-3.36 p = 0.036) (see Table I). Several studies have had a similar result, including an Ethiopian study by Panela et al. in 2014 (RR: 1.48, CI: 95%: 1.02-2.14), de Brennan et al. , Gupta et al. In South Africa in 2013 (RR: 1.2 95% CI: 1.1-1.2), a Mexican study by Martin –Echevarria et al. in 2014 also that of Dar es Salaam in Tanzania by Liu et al. in 2015

predicting males to be at greatest risk of developing TB within the first six months of initiating ART. TB presents itself as a disease that predominantly affects males. On the one hand, social behavior and hormonal differences between the susceptibility of men and women to developed TB have been suggested as a possible explanation for the prevalence of TB in adult men. On the other hand, the difference in Gender in the susceptibility to develop TB is clinically important since it has been shown that male patients have a higher risk of mortality [Gupta, A 2012, Panela, P 2014; ABGRALL 2008, Echevarria, E. M. 2014.]. [3, 5, 10,13].

The results of our study showed that marriage is associated with the onset of TB (OR = 3.7 95% CI: 1.005-13.5 p = 0.049) (See Table I) .Congruent findings have already been reported in other countries, like that made by Yihun et al. in Burkina Faso assigning a very high risk to married patients. Indeed, it is difficult to establish with certainty the link between TB and marriage. However, we think it shows in the idea that those who marry and stay united have the advantage of contaminating themselves because of the importance of promiscuity with the spouse living in the same house. [6]. Studies in The Gambia and Guinea Bissau have reported contrary results where divorced and widowed patients were at higher risk of developing TB within the first six months of initiating ART. Marriage has a negative effect on the transmission of TB, in that those who marry have better health because of the positive psychological and social impact [3]

In our study, we found that stages 3 and 4 are associated with the occurrence of TB in PLWHA (OR = 17 95% CI: 3.3-90.5 p = 0.001 and OR = 25 95% CI %: 2.3-275.4 p = 0.009 respectively) (See Table II) .This study is in agreement with several other studies, for example, in 2015 by Lawn et al. in South Africa reported that patients who had started ART at clinical stages 3 and 4 of WHO were 3.6 times more likely to have TB. [14] another study in Ethiopia by

Melkanu et al. Found that the development of active TB was significantly higher in patients in WHO clinical stages 3 and 4 compared to those in clinical stages 1 and 2 (OR = 2.29,; p = 0.003) [4]. Also similar to those found by Panela et al. in Burkina-Faso and Abgrall et al. in France who have shown that the risk was higher in stage IV patients (RR: 6, 41, 95% CI: 2.86-14.38) [5, 10]. This could be explained by the fact that once patients reach an advanced stage, the immune defense capacity will be minimal, which would expose them to TB infection. It should also be mentioned that TB is one of the criteria for defining AIDS for classify patients in the WHO clinical classification. Where they came from in the advanced stages of AIDS.

This shows the importance of implementing the innovation of algorithms for active tuberculosis research in PLWHIV as recommended by the PNLT

Conclusion

The predictive factors for the occurrence of tuberculosis in PLWHA on ART are: being married, living in Tshopo Municipality, clinical stages 3 and 4 of AIDS disease. Our results underscore the need for active tuberculosis research among PLHIV in African cohorts. special emphasis will be placed on the category of patients mentioned above, that is to say those with one of the factors independent of the occurrence of TB on ART

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Table I: Comparison of the socio-demographic characteristics of cases and controls of HIV-TB co-infection

Variables	Cas, N=58(%)	Témoins, N=174(%)	OR (IC 95%)	P-value
Age				
15-24	1(1,7%)	11(6,3%)	0,2(0,03-2,9)	0,199
25-34	14(24,14%)	38(21,84%)	0,2(0,2-4,2)	0,0339
35-44	24(41,38%)	70(40,2%)	0,3(0,02-4,5)	0,363
45-55	15(25,9%)	34(19,5%)	0,7(0,21-2,2)	0,405

≥ 5	54 (6,8 %)	8 (4,6 %)	2,8 (0,28-26,6)	0,382
Sexe				
Masculin	**30 (51,7 %)**	**64 (36,8 %)**	**1,8 (1,01-3,36)**	**0,036**
Féminin	28 (48,3 %)	110 (63,2 %)	0,7 (0,5-0,9)	0,036
Etat-civil				
Marié	**32 (55,2 %)**	**84 (48,3 %)**	**3,7 (1,005-13,5)**	**0,049**
Célibataire	22 (37,9 %)	51 (29,3)	1,2 (0,6-2,3)	0,564
Divorcé	3 (5,2 %)	24 (13,8 %)	0,2 (0,02-1,4)	0,098
Veuf (ve)	1 (1,7 %)	15 (8,6 %)	0,1 (0,18-1,2)	0,069
Résidence				
Makiso	7 (12,1 %)	52 (29,9 %)	0,2 (0,08-0,59)	0,003
Tshopo	**18 (31 %)**	**30 (17,2 %)**	**7 (1,08-42,5)**	**0,033**
Kabondo	19 (32,8 %)	50 (28,7 %)	1,2 (0,2-6,7)	0,805
Mangobo	8 (13,8 %)	15 (8,6 %)	0,28 (0,06-1,4)	0,118
Lubunga	4 (6,9 %)	15 (8,6 %)	0,4 (0,08-1,99)	0,268
Kisangani	2 (3,4 %)	12 (6,9 %)	0,3 (0,06-1,8)	0,186

Table II: Clinical stages of AIDS

Variables	Cas, N=58(%)	Témoins, N=174(%)	OR (IC 95%)	P-value
Stades cliniques de SIDA				
Stade 1	1 (1,7%)	20 (11,5%)	0,7(0,07-6,5)	0,744
Stade 2	3 (5,2%)	56 (32,2%)	0,09(0,01-0,7)	0,026
Stade 3	49 (84,5%)	94 (54%)	17(3,3-90,5)	0,001
Stade 4	5 (8,6%)	4 (2,3%)	25(2,3-275,4)	0,009

Table III: Predictors of TB onset in PLWA on ART: univariate and multivariate analysis

Variables	CasN=58(%)	Témoins, N=174(%)	OR brute (IC à 95%)	OR ajusté (IC à 95%)	P – value
Sexe					
Masculin	30(51,7%)	64 (36,8%)	1,8 (1,01-3,36)	0,5 (0,257-1,033)	0,062
Féminin	28(48,3%)	110 (63,2%)	1	1	
Etat civil					
Marié	32(55,2%)	84 (48,3%)	3,7 (1,005-13,5)	4,5 (1,06-18,7)	0,041
Célibataire	22(37,9%)	51 (29,3%)	1,2 (0,6-2,3)	1,3 (0,635-2,829)	0,389

Variables	CasN=58(%)	Témoins, N=174 (%)	OR brute (IC à 95%)	OR ajusté (IC à 95%)	P – value
Divorcé	3 (5,2)	24 (13,8)	0,2 (0,02-1,4)	0,13 (0,014-1,225)	0,075
Veuf	1 (1,7%)	15 (8,6%)	1	1	
Résidence					
MAKISO	7 (12,1%)	52 (29,9%)	0,2 (0,08-0,059)	0,7 (0,122-4,536)	0,750
TSHOPO	18 (31)	30 (17,2)	7 (1,08-42,5)	7,04 (1,168-42,47)	0,033
KABONDO	19 (32,8%)	50 (28,7%)	1,2 (0,2-6,7)	0,2(0,044-1,357)	0,101
MANGOBO	8 (13,8%)	15 (8,6%)	0,28 (0,06-1,4)	0,47(0,103-2,163)	0,333
LUBUNGA	4 (6,9)	15 (8,6)	0,4 (0,08-1,99)	0,35 (0,047-2,617)	0,307
KISANGANI	2 (3,4)	12 (6,9)	1	1	
STADE CLINIQUE					
STADE 1	1 (1,7%)	20 (11,5%)	1	1	
STADE 2	3 (5,2)	56 (32,2)	0,09 (0,01-0,7)	0,069 (0,008-0,578)	0,014
STADE 3	49 (84,5%)	94 (54%)	17 (3,3-90,5)	29 (4,56-184,87)	0,000
STADE 4	5 (8,6%)	4 (2,3%)	25 (2,3-275,4)	50,8 (3,79-680,995)	0,003