

## Original Research Article

### **HIV infection in patients with tuberculosis followed and treated at the Oyem Regional Hospital Center (ORHC) : A 2-year retrospective study in Northern Gabon.**

#### **Abstract**

**Background:** The objective of this study was to investigate HIV infection in patients with tuberculosis followed and treated at the Oyem Regional Hospital Center (ORHC).

**Materials and Methods:** Based on the exploitation of medical records and data registers of the medical analysis laboratory of the said hospital centre, this retrospective and descriptive study was conducted from January 2020 to December 2021. Only patients diagnosed with tuberculosis, confirmed by positive culture on Lowenstein Jensen agar medium, and diagnosed with HIV infection, confirmed by Western blot, were included.

**Results:** In this study, 128 confirmed cases of tuberculosis were selected. Of these, 54 (42.18%) had confirmed HIV infection. While thirty (23.43%) co-infected patients had extra pulmonary TB and 24 (18.75%) had pulmonary TB, 43 (33.59%) mono-infected patients had pulmonary TB and 31 (24.21%) had extra pulmonary TB. The patients were put on anti-tuberculosis treatment according to the manufacturers' indications. Despite a total of 15 deaths (11.72%) in mono- and co-infected patients, there was a favourable evolution, with 35 patients (27.34%) declared cured. With 8 (6.25%) deaths, mortality was higher in co-infected patients than in HIV-uninfected TB patients, who recorded 7 (5.47%) deaths ( $p < 0.05$ ).

**Conclusion:** By indicating a relatively high prevalence of HIV infection in TB patients, this study showed that TB+/HIV+ co-infection was associated with extra pulmonary TB, the severe form of the disease, and increased mortality in patients, hence the need to strengthen joint activities to control this co-infection.

**Key words:** Infection, Co-infection, TB, HIV, Tchibanga, Northern, Gabon

**Comment [MSMM1]:** It's better if you can write 1-2 lines about the background of your topic/problem.

**Comment [MSMM2]:** Did you obtain ethical approval?

**Comment [MSMM3]:** Is there any exclusion criteria?

**Comment [MSMM4]:** usually it is suggested to write in words when it is first word. in this case your sentence is starting with While so you can write 30 instead of thirty.

**Comment [MSMM5]:** Please specify co-infections.

**Comment [MSMM6]:** If you started with extra pulmonary TB in first statement then in next I would suggest again to write extra pulmonary TB first and pulmonary second.

**Comment [MSMM7]:** Can you please explain this statement? treatment according to the manufacturers indications?

**Comment [MSMM8]:** I suggest to write these results in a more clear way.

**Comment [MSMM9]:** Please rewrite.

## I. Introduction

The COVID-19 pandemic has reversed years of global progress in TB control and, for the first time in more than a decade, TB deaths have increased, according to the World Health Organization's (WHO) Global TB Report 2021 [1]. The WHO estimates that in 2018, 1.5 million people died from TB, more than from any other single infectious agent [2]. TB is present in all regions of the world. In 2020, the WHO region with the highest number of new TB cases was South-East Asia (43% of all new cases), followed by the African Region (25%) and the Western Pacific Region (18%) [1]. In recent years, HIV infection is a major risk factor for *Mycobacterium tuberculosis* infection. It is the most common cause of AIDS-related deaths [3]. For example, approximately 1.5 million people died from TB in 2020 (214,000 of whom were HIV-positive) [1]. With an incidence estimated by the World Health Atlas in 2019 at 521 per 100 000 inhabitants for tuberculosis [4], and an estimated national prevalence of 4.1% for HIV infection [5], Gabon is not immune to the ravages of TB/HIV co-infection. According to the WHO Stop TB/HIV programme, surveillance of TB/HIV co-infections is recommended to plan joint activities to combat TB and HIV infection [6]. Although there are few studies conducted in other regions of Gabon, none have focused on the prevalence of tuberculosis (TB) and TB/HIV co-infection in our study area. It is in this context that the Regional Hospital of Oyem in northern Gabon was used as a setting to study HIV infection in patients with confirmed tuberculosis who are followed and treated there.

**Comment [MSMM10]:** I think it's better to start writing introduction with HIV and TB instead of COVID-19. Introduction should be started with problem statement.

**Comment [MSMM11]:** How is HIV a major risk factor for Tuberculosis? Can you please explain it?

**Comment [MSMM12]:** TB is the most common cause of AIDS related deaths or is it the other way?

**Comment [MSMM13]:** In third line of introduction it is mentioned that 1.5 million people were died with TB in 2018 and here in this statement 1.5 million people died in 2020, does it mean that the mortality did not increase in 2 years? If so, Please justify line 3-4 of the introduction.

## II. Materials and Methods

### 2.1. Data collection

This was based on the exploitation of medical records and registers of results from the medical analysis laboratory of the regional hospital of Oyem. Only patients with culture-positive tuberculosis on Lowenstein Jensen agar medium and HIV infection confirmed by Western blot between January 2020 to December 2021 were included.

### 2.2. Data analysis

The data were entered in Microsoft Excel 2016 and then analysed using R software version 3.6.1. A Binomial test following the Normal distribution was used to compare the percentages. A 95% confidence interval was estimated and a p-value  $\leq 0.05$  was considered statistically significant.

### 2.3 Ethical considerations

To avoid stigmatisation, the data received did not include the identity of the patients or any personal information.

## III. Results

### III-1 Prevalence and distribution of mono-infection (TB+/HIV-), and TB+/HIV+ co-infection in the study population.

A total of 128 cases of tuberculosis (TB) confirmed by culture on Lowenstein Jensen agar medium were included in this study. Of these, 54 (42.18%) cases were diagnosed as positive for HIV infection and confirmed by Western blot. With an average of 34.5 years in both mono-infected (TB+/HIV-) and co-infected (TB+/HIV+) patients, the age group 30-39 years (46.3%) was the majority with percentages of 23.44% and 19.53%, with male predominance Table 1.

**Table 1:** Prevalence and distribution of mono-infection (TB+/HIV-), and TB+/HIV+ co-infection according to Gender and age groups, in the study population.

Variables	TB+/HIV-		TB+/HIV+	
	Numbers	%	Numbers	%
<b>Gender</b>				
Male	56	43.75	38	29.69
Female	18	14.06	16	12.5
<b>Age groups (years)</b>				
$\leq 19$	1	0.78	0	0
20-29	7	5.47	5	3.90
30-39	30	23.44	25	19.53
40-49	21	16.41	17	13.28
$\geq 50$	15	11.72	7	6.47

### III-2. Distribution of clinical forms of tuberculosis in TB+/HIV- and TB+/HIV+ co-infected patients in the study population

The study of the different clinical forms of tuberculosis indicated the presence of extra-pulmonary tuberculosis in 43 co-infected patients, compared to 11 for pulmonary tuberculosis. In the mono-infected patients, pulmonary tuberculosis was found in 24 cases compared to 50 with extra

**Comment [MSMM14]:** I think it's better not to write mono-infection and co-infection and you can only mention TB patients with and without HIV. When you say mono-infection it means patients don't have any other infection with HIV, or you should write a clear exclusion criteria that you have excluded people with every other possible co-infection for example HCV, HBV...

**Comment [MSMM15]:** detected

**Comment [MSMM16]:** HIV infection by western blot

**Comment [MSMM17]:** Highest prevalence of both mono-infected and co-infected patients was found in patients between 30-39 years of age, while the mean age was 34.5 years.

**Comment [MSMM18]:** 0.78

pulmonary tuberculosis. Furthermore, the analysis of the level of significance of the differences observed in the percentage of TB infection of TB+/HIV mono-infected patients compared to TB+/HIV+ co-infected patients in the study population according to pulmonary or extra pulmonary TB was carried out using the exact binomial test, with a 95% confidence interval. As the test was considered significant when p-value  $\leq 0.05$ , table 2 shows that TB+/HIV+ co-infection was significantly associated with extra pulmonary TB.

**Table 2:** The different clinical forms of tuberculosis in TB+/HIV- and TB+/HIV+ co-infected patients in the study population.

Clinical forms of TB	TB+/HIV-	TB+/HIV	Total	Binomial test		
				p(TB+/HIV+)	IC95%	p-value
Pulmonary	24	11	35	0.27	[0.2 - 0.3]	
Extra pulmonary	50	43	93	0.72	[0.5 - 0.8]	<0.05*
Total	74	54	128	0.57	[0.48 - 0.6]	

\* Significant test

**Comment [MSMM19]:** this means HIV is present in almost half of the extra pulmonary TB patients?

### III-3. Therapeutic outcomes of patients after anti-TB and antiretroviral treatment

57.81% (n=74) mono-infected (TB+/HIV-) and 42.19% (n=54) co-infected (TB+/HIV+) patients were put on anti-tuberculosis treatment according to the manufacturer's indications. Among the mono-infected (TB+/HIV-), the therapeutic success, with declaration of cure, was 26 (20.31%) patients, 23 (17.97%) patients were undergoing treatment, the percentage of patients who abandoned the treatment was 14.07% (n=18), finally, 7 (5.47%) deaths were recorded. Among the co-infected, the therapeutic success with declaration of cure was 7.03% (n=9). 25 (19.53%) patients were undergoing treatment. 12 patients (9.37%) had dropped out or were lost to follow-up. Finally, the number of deaths was 8 (6.25%).

**Comment [MSMM20]:** seventy-four (57.81%)

**Comment [MSMM21]:** What do you mean by treatment according to manufacturer's indications?

**Table 3:** Therapeutic outcomes of patients with tuberculosis.

Outcomes	TB+/HIV-		TB+/HIV+	
	(n=74)	%	(n=54)	%
Reported cured	26	20.32	8	7.03
Ongoing treatment	23	17.97	25	19.53
Discontinued and lost to follow-up	18	14.01	12	9.37
Deaths	7	5.47	8	6.25

**Comment [MSMM22]:** Please rewrite in a clear manner to make it more understandable. You can mention treatment response rate instead of cure and ongoing treatment.

**Comment [MSMM23]:** The table can be modified according to above mentioned suggestion about replacing reported cure to treatment respondents and non respondents.

#### IV. Discussion:

With the objective of studying HIV infection among TB patients followed up at the Oyem Regional Hospital Centre (ORHC), contrary to the results obtained in Morocco 39.3%, Brazil 27.7%, Cameroon 26.06%, Togo 23.7% and even Korea 15.9% [7, 8, 9, 11, 12], this study indicated a relatively high prevalence of HIV infection among TB patients (42.18%). This result could be explained by the fact that the northern region of Gabon borders Cameroon and Equatorial Guinea. It is a place where populations from different backgrounds mix and contamination due to promiscuity can be high. With 55 patients and a rate of 42.97%, patients in the 30-39 age group were more mono infected than co-infected, compared to other age groups. This result, although higher, is not far from the 34.24% found elsewhere in the 30-39 years old age group of TB/HIV co-infected patients [13]. This correlates well with the fact that this age group constitutes a category of young active adults, more often infected with most transmissible diseases such as TB or most often affected by HIV/AIDS, but more aware and active in the therapeutic follow-up of the infection [14]. Similarly, in a guide for the management of TB/HIV co-infection of the National Tuberculosis Control Programme of the Republic of Congo in 2020, this study indicates that TB+/HIV+ co-infection was significantly associated with severe tuberculosis (extra pulmonary tuberculosis) and an increased mortality rate among tuberculosis patients; this is in line with the results of studies obtained in a previous study [15]. This correlates well with the fact that once depressed by HIV, a patient with even latent TB is at risk of developing more active TB. With regard to therapeutic outcomes, the results obtained after anti-tuberculosis treatment in this study are far from meeting the expectations of the WHO, whose targets for 2030 are to reduce the number of deaths due to tuberculosis and its co-infection with HIV by 90%, and to reduce the incidence of the disease (number of new cases per year per 100,000 inhabitants) by 80% compared to 2015 [1]. With the overall cure rate of TB ranging from 71.1 to 74.4% depending on the prevalence of HIV infection in Africa [16], our study showed a 20.31% (n=26) higher cure rate in mono-infected patients than in co-infected patients 7.03% (n=9). This may be explained by the fact that co-infected patients in this study may have lower than normal CD4 counts which complicate treatment and the high frequency of drug intolerance observed in HIV-positive patients and drug interactions between anti-tuberculosis drugs (especially rifampicin) and some antiretrovirals [16]. In total, many patients (37.5%)

Comment [MSMM24]: .

were still on treatment at the time of this study. This can be explained by the heavy and long duration of the TB treatment, as each TB patient is usually treated according to a treatment regimen of several months, divided into 2 phases [17]. Although at a national seminar, the Director of the National Tuberculosis Control Programme in Gabon (PNLT) mentioned a shortage of 40% of TB patients who had dropped out of treatment and were lost to follow-up, which was disseminated throughout the country [13], this study found a relatively low treatment drop-out rate, both among mono-infected patients (14.07%) and among co-infected patients (9.37%). These results are contrary to those of a previous study which found a drop-out rate of 21.5% [18]. This result can be explained not only by the fact that the Gabonese government and its partners cover the cost of the BCG vaccine, to begin with during the first few months of birth, but also by the fact that the geographical location of the treatment centres is close to the population, and that the cost of anti-tuberculosis treatment and the acquisition of antiretroviral drugs are free. The overall cure rate for TB varies from 71.1% to 74.4% in Africa, depending on the prevalence of HIV infection [15]. The mortality rate in this study was 6.25% (n=8) in co-infected patients and 5.47% (n=7) in mono-infected patients, indicating an impact of HIV infection on mortality in TB patients. These results are superimposed on those found elsewhere, which showed that TB mortality was higher in co-infected patients than in mono-infected patients [18]. Due to the confidence in the traceability of the registers made available to us for this study, no TB drug resistance was recorded in the course of this work.

### Limitations of the study

This study was marked by the absence of certain important data in the registers made available to us. We had to subtract missing data such as biological or socio-economic and demographic data necessary for the study. As the viral load was not available for all patients for technical reasons, we removed this parameter. Finally, the present study is a hospital-based analysis of patients infected with TB and the results may not be generalizable.

### Conclusion:

Despite the fact that the Gabonese government has made the fight against HIV/AIDS a priority in its national health policy, the prevalence of co-infection with tuberculosis and HIV among tuberculosis patients is still high in our study region. In addition to strengthening preventive measures relating to screening, diagnosis, treatment and follow-up, the fight against this burden should also consider not only the socio-economic factors of HIV patients, but also the genetic and molecular markers associated with TB/HIV co-infection.

**Comment [MSMM25]:** Suggestion for conclusion: The study concluded that the prevalence of HIV in TB patients is higher than the prevalence of HIV in general population of Gabon. Moreover, we observed that the TB patients with HIV co-infection were more resistant to anti-tuberculosis therapies and vice versa.

## References

1. World Health Organization: Tuberculosis deaths are on the rise for the first time in more than a decade due to the COVID-19 pandemic. October 14, 2021 Press release Geneva
2. Zaheen A, Bloom BR. Tuberculosis in 2020 - New Approaches to a Continuing Global Health Crisis. *N Engl J Med.* 2020 Apr;382(14):e26. doi: 10.1056/NEJMp2000325. PMID: 32242354.
3. Canetti D, Riccardi N, Martini M, Villa S, Di Biagio A, Codecasa L, Castagna A, Barberis I, Gazzaniga V, Besozzi G. HIV and tuberculosis: The paradox of dual illnesses and the challenges of their fighting in the history. *Tuberculosis (Edinb).* 2020 May;122:101921. doi: 10.1016/j.tube.2020.101921. Epub 2020 Mar 25. PMID: 32501257.
4. World Health Atlas 2018
5. Medias241 HIV/AIDS: 51,000 PEOPLE INFECTED IN GABON DECEMBER 1, 2020
6. Guide to monitoring and evaluation of collaborative TB/HIV activities, Revision 2015 WHO. Google Scholar
7. Kettani AE, Jebbar S, Takourt B, et al. HIV co-infection in patients followed up for tuberculosis in the Division of Infectious Diseases at the Ibn Rochd University Hospital in Casablanca [HIV co-infection in patients followed up for tuberculosis in the Division of Infectious Diseases at the Ibn Rochd University Hospital in Casablanca]. *Pan Afr Med J.* 2018;30:276. Published 2018 Aug 16 doi:10.11604/pamj.2018.30.276.13913
8. Castro Castrighini C, Reis RK, Souza Neves LA, Galvão MTG, Gir E. Epidemiological profile of HIV/Tuberculosis co-infection in a City in the State of São Paulo, Brazil. *J Antivir Antiretrovir.* 2013; 5(5): 119-122.
9. Noubom M, Nemboi FD, Donfack H, Mfin PSK, Tchasse F. Characteristics of tuberculosis patients in western Cameroon: 2000-2009. *Pan Afr Med J.* 2013; 16:39. PubMed | Google Scholar
10. El Kamel A, Joobeur S, Skhiri N, Cheikh Mhamed S, Mribah H, Rouatbi N. The fight against tuberculosis in the world. *Rev Pneumol Clin.* April 2015; 71(2-3): 181-187
11. Lee CM, Lee E, Bang JH, et al. Prevalence of Multidrug-Resistant Tuberculosis in HIV/Tuberculosis Co-Infected Patients. *Infect Chemother.* 2021;53(4):792-795. doi:10.3947/ic.2021.0085
12. K. Adjoh • S. Tchaptchet Heunda • A.A. Patassi • D. Sadzo Hetsu • F. Awokou • O. Tidjani Prevalence of HIV-TB co-infection and impact of HIV infection on pulmonary tuberculosis outcome in Togo A.Y. Dagnra • Bull. Soc. Pathol. Exot. (2011) 104:342-346 DOI 10.1007/s13149-010-0079-3
13. Thierry Ndong Mba, Cedric Sima Obiang, Patrick Mickala et al. Epidemiological and Clinical profile of HIV/TB co-infected patients in two departments of the Ngounié province in Southern Gabon International Journal of Innovation Scientific Research and Review Vol. 03, Issue, 07, pp.1489-1493, July, 2021 Available online at <http://www.journalijisr.com>

14. UNIES, N. and C.E.E. SOCIAL, The female dimension of HIV/AIDS in Africa. 2004
15. Guide to the management of TB/HIV coinfection of the National Tuberculosis Control Program of the Republic of Congo in 2020
16. Dye C, Watt CJ, Bleed DM, et al (2005) Evolution of tuberculosis control and prospects for reducing tuberculosis incidence, prevalence, and deaths globally. *JAMA* 293(22):2767–75
17. Fujiwara PI, Clevenbergh P, Dlodlo RA. Management of adults living with HIV/AIDS in low-income, high-burden settings, with special reference to persons with tuberculosis. *Int J Tuberc Lung Dis* 2005;9:946–58. [Medline]
18. Rakotonirina, El-C. Julio, et al. "Factors associated with the abandonment of anti-tuberculosis treatment in the city of Antananarivo, Madagascar", *Santé Publique*, vol. 21, no. 2, 2009, p. 139-146.
19. Matos, e. d. lemos, a. c, bittencourt, c. mesquita, c. I. & kuhn, p. vs. 2007. Prevalence of HIV infection in patients hospitalized for tuberculosis in Bahia, Brazil. *Braz J Infect Dis*, 11, 208-11

UNDER PEER REVIEW