

## Epidemiological, Clinical, Evolutive and Prognostic Aspects of Tuberculosis HIV Co-Infection in the Gbeke Region in Côte D'ivoire

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### ABSTRACT

**Introduction:** TB/HIV co-infection is a major health problem in Africa. This co-infection is associated with high mortality and additional therapeutic challenges. This study aimed to determine current aspects of tuberculosis in TB/HIV patients.

**Materials and method:** We carried out a retrospective, descriptive and analytical study over a period of 4 years. We used the medical records of TB/HIV patients from the Gbêkê region. Data analysis was performed with Epi Info 3.2.1 software.

**Results:** The prevalence of HIV in tuberculosis patients was 18.7%. The average age of the patients was 37 years old. The female gender (60%) predominated. The patients lived as a couple in 49.1%. Nurses accounted for 2.6%. Pulmonary tuberculosis (79.3%) was predominant. The extra-pulmonary forms were dominated by pleural (45.3%) and lymph node (32.4%) tuberculosis. The site of infection was unique (74.4%) and drug-resistant forms accounted for 3.1%. All the patients screened were immediately put on anti-tuberculosis treatment, only 94.8% had been put on antiretroviral treatment. Mortality was 18.7%. The determinants of mortality were the age group from 5 to 14 years ( $p < 0.001$ ), female gender ( $p = 0.04$ ), civil servant patients ( $p < 0.001$ ), patients without profession ( $p < 0.001$ ), pleural tuberculosis ( $p = 0.04$ ) and neuromeningeal tuberculosis ( $p = 0.011$ ).

**Conclusion:** Prevalence and mortality remain high in TB/HIV patients. Tuberculosis was more deadly in adolescents, women, civil servants, the unemployed, the pleural and neuromeningeal form.

### Keywords

Tuberculosis, HIV, Gbêkê /Ivory Coast, GeneXpert.

### Introduction

Tuberculosis (TB) is a contagious infectious disease caused by mycobacteria of the tuberculosis complex, the most common of which is *Mycobacterium tuberculosis* (Koch's bacillus). It mainly affects the lungs, but can also affect other organs. The human immunodeficiency virus (HIV) weakens the body's immune

system, making people infected with HIV more susceptible to infections, including tuberculosis [1]. According to the World Health Organization (WHO), tuberculosis is one of the ten leading causes of death worldwide [2]. In 2020, there were approximately 9.9 million new cases of TB globally, which is an increase from previous years. TB/HIV co-infection is also a major health problem in Africa, where approximately 1.4 million people were co-infected in 2020. This co-infection is associated with higher mortality and treatment difficulties additional [2]. According to

data from the National Tuberculosis Control Program (PNLT), in Côte d'Ivoire in 2020, the prevalence of TB/HIV co-infection was 24% [3]. People who are co-infected have a higher risk of mortality than people infected with TB alone [1]. Additionally, this co-infection can make treating TB more difficult, as co-infected patients are more likely to experience side effects and not respond to treatment [4]. To fight against TB/HIV co-infection in Côte d'Ivoire, the National Program for the Fight against Tuberculosis (PNLT) and the National Program for the Fight against AIDS (PNLS) supported by the State and the global fund are working to improve the detection and management of both diseases [3,5]. People who are co-infected should receive antiretroviral treatment and anti-tuberculosis treatment simultaneously to improve their chances of recovery. Initiatives such as building the capacity of integrated HIV and TB testing and treatment centers are underway to improve patient care [6]. Since 1998, no study has focused on TB/HIV co-infection in the Gbêkê region [7]. It is in this context that we are conducting this study to determine the current aspects of TB among people living with HIV in the Gbêkê region in the context of the COVID-19 pandemic. This study will make it possible to update the data on the aspects of TB among people living with HIV in the region and to organize the joint fight of the TB/HIV couple.

## Material and Methods

We carried out this descriptive and analytical retrospective study over a period of 4 years, from January 2019 to December 2022. It focused on the medical records of patients co-infected with tuberculosis and HIV in the anti-tuberculosis centers of the health region of Gbeke. This region is located in the center of the country, it is made up of six health districts and a University and University Hospital Center (CUTH). It includes five towns (Bouaké, Béoumi, Sakassou, Botro and Brobo) and twenty tuberculosis treatment centres. The pneumophtisiology department of the Bouaké University Hospital and the Anti-Tuberculosis Center are the two main reference centers for the management of complicated cases in the region and the bordering regions of the centre, north and west of the country. The area of the Gbêkê region is estimated at 10,429 km<sup>2</sup>, with an estimated population of 1,314,621 inhabitants, a population density of 120 inhabitants/km<sup>2</sup> [8]. It is the second health region of the country in terms of population density after the region of Abidjan. Sputum from suspected TB patients and other biological secretions were collected at health centers by health workers (doctor, nurses, midwives, caregivers) and transported by trained caregivers or community health workers to screening centers for the diagnosis of tuberculosis. Sometimes, some patients were referred directly to these collection and management centers for various reasons (difficulties of access, complications, lack of inputs, etc.). The sputum and biological fluids were analyzed by the molecular biology technique with the GeneXpert device or by microscopy after Ziehl Nielsen staining in certain centres. The HIV rapid diagnostic test (determine, STAT-PAK) was systematically performed in all patients. Patients who tested positive for TB were immediately put on anti-TB treatment. Cases of extrapulmonary tuberculosis and clinically diagnosed tuberculosis were left to the discretion of the physician according to national recommendations.

The treatment was either given directly to the patients or to their companion after explanation of the dosage and duration, or when the patient was absent, the treatment was entrusted to the trained community counselor to give it to the patient either at home or at the health center of the hospital where the sample was taken. All patients diagnosed with TB were followed by a community health worker and a close relative, who were responsible for supervising drug intake and adherence to follow-up appointments as part of the DOTS strategy. The duration of treatment was at least six months. The therapeutic protocol was two months of Rifampicin+Isoniaside+Pyrazinamide+Ethambutole (2RHZE) and four months of Rifampicin+Isoniaside (4RH) and sputum control at the 2nd, 5th and 6th month of treatment according to the national recommendation. When the HIV tests were positive, the patient was cared for on site in HIV care centers or referred by the doctor or nurse to an HIV care center. Patients were accompanied by community health workers to these HIV treatment centres.

Pulmonary tuberculosis has been defined as the localization of tuberculosis in the lung parenchyma, including miliary tuberculosis. Extrapulmonary tuberculosis was defined as the location of tuberculosis outside the lung parenchyma. Bacteriologically confirmed tuberculosis was all forms of tuberculosis with isolation of Mycobacterium by baccilloscopy or geneXpert. Tuberculosis diagnosed clinically was all the forms of tuberculosis for which the germ was not found, but the strong clinical and radiological suspicion and the good evolution under antituberculous treatment had made it possible to retain the diagnosis. Treatment failure was any case that continued to show positive results (as determined by smear examination or culture) after five or more months of treatment. Cure was defined as any patient with pulmonary tuberculosis whose condition was bacteriologically confirmed at the start of treatment and who had presented negative results (according to smear or culture) during the last month of treatment and at least once before. Completed treatment was any TB patient who completed treatment without evidence of failure, but there is no evidence of negative smear or culture results in the last month of treatment. Treatment and at least once before, either because the tests were not carried out or because results are not available. Therapeutic success was the sum of patients cured and patients who completed their treatment. The lost to follow-up patient was the one who had not started treatment or who had interrupted treatment for two or more consecutive months. The unassessed treatment case was any TB patient for whom no treatment outcome was assigned. This category includes cases transferred to another treatment unit and those whose results are unknown to the reporting unit.

The study population consisted of all patients who had been followed and treated for tuberculosis during the study period in the various tuberculosis care centers in the region. From this population, we included all patients infected with newly discovered or old HIV. We did not include patients who did not have a complete medical file for the parameters studied. The data was collected from the medical files of the patients with an investigation form established for the circumstance. We proceeded

to an exhaustive sampling, which enabled us to retain 864 records of patients infected with HIV and tuberculosis. The parameters collected were socio-demographic characteristics, clinical forms, evolutionary characteristics and HIV status. This study was carried out with the agreement of the health authorities of the Gbêkê region and the managers of the various tuberculosis and HIV treatment centres. Data analysis and interpretation were performed with Epi Info version 3.2.1 software. Quantitative variables were expressed as mean with standard deviation and extreme values. Qualitative variables were expressed as a proportion. The significance threshold for the statistical tests was set at a value of  $p \leq 0.05$ .

## Results

Out of a total of 4621 patients infected with tuberculosis and followed up in tuberculosis care centers in the Gbêkê region, 864 patients were infected with HIV, i.e. a prevalence of 18.7% (Table 1).

**Table 1:** Annual frequency of TB and TB-HIV in the Gbêkê region.

Year	TB patients	TB-HIV patients	TB-HIV percentage
2018	955	216	22.6%
2019	983	180	18.3%
2020	799	140	17.5%
2021	943	175	18.6%
2022	941	153	16.3%
Total	<b>4621</b>	<b>864</b>	<b>18.7%</b>

## Socio-Demographic Characteristics

The average age of the patients was  $37 \pm 14$  years [extremes of 6 months and 73 years], the age group of tuberculosis patients from 25 to 49 years (72.2%) was the most infected with HIV. Female patients were in the majority (60%) and the sex ratio was 0.67. Patients lived as a couple in 49.1% of cases. Care staff represented 2.6% of patients infected with tuberculosis and HIV (Table 2).

**Table 2:** Sociodemographic characteristics of TB-HIV patients.

Variables	Total n = 864 (%)	Deceased patients n = 162 (%)	non-deceased patients n = 702 (%)	p -Value
Age				
[0-4 years]	22 (2.6%)	3 (1.9%)	19 (2.7%)	0.729
[5-14 years]	14 (1.6%)	7 (4.3%)	7 (1%)	<b>&lt;0.001</b>
[15-24 years old]	49 (5.7%)	11 (6.8%)	38 (5.4%)	0.620
[25-49 years old]	624 (72.2%)	112 (69.1%)	512 (72.9%)	0.381
≥ 50 years	155 (17.9%)	29 (17.9%)	126 (18%)	0.988
Sex				
Feminine	518 (60%)	105 (64.8%)	393 (56%)	<b>0.04</b>
Male	346 (40%)	57 (35.2%)	309 (44%)	
Marital status				
Couple	423 (49%)	69 (42.6%)	354 (50.4%)	0.07
Bachelor	328 (38%)	69 (42.6%)	259 (36.9%)	<b>0.178</b>
Widowed	53 (6.1%)	11 (6.8%)	42 (6%)	0.699
Divorced	4 (0.5%)	1 (0.6%)	3 (0.4%)	1,000
Unspecified	56 (6.4%)	12 (7.4%)	44 (6.3%)	0.595
Professional activities				
Liberal activity	365 (46.9%)	65 (40.1%)	300 (42.7%)	0.544
Officials	335 (42.2%)	12 (7.4%)	323 (46%)	<b>&lt;0.001</b>
No occupation	103 (4.5%)	70 (43.2%)	33 (4.7%)	<b>&lt;0.001</b>
Pupils/Students	39 (3.8%)	9 (5.6%)	30 (4.3%)	0.478
Health workers	22 (2.6%)	6 (3.7%)	16 (2.3%)	0.299

## Clinical Features

The pulmonary form of tuberculosis including miliary tuberculosis (79.3%) was predominant in HIV-infected patients. Extra-pulmonary forms were dominated by pleural tuberculosis (45.3%) and lymph node tuberculosis (32.4%). The infectious focus was unique in 74.4% and drug-resistant forms represented 3.1% of cases (Table 3).

**Table 3:** Clinical forms of tuberculosis in HIV-infected subjects.

Variables	Total n = 864 (%)	Deceased patients n = 162 (%)	non-deceased patients n = 702 (%)	p -Value
Clinical forms				
TPB+*	<b>252 (29.2%)</b>	<b>43 (26.5%)</b>	<b>209 (29.8%)</b>	0,472
TPB-***+ Military	<b>433 (50.1%)</b>	<b>91 (56.2%)</b>	<b>342 (48.7%)</b>	<b>0,08</b>
PET***	<b>179 (20.7%)</b>	<b>28 (17.3%)</b>	<b>151 (21.5%)</b>	0,231
• Plural	81 (45.3%)	7 (25%)	74 (49%)	<b>0,019</b>
• lymph node	58 (32,4%)	12 (42,8%)	46 (30,5%)	0,198
• Peritoneal	17 (9,5%)	3 (10,7%)	14 (9,3%)	0,810
• bone	11 (6,1%)	1 (3,6%)	10 (6,6%)	0,541
• Meningeal	7 (3,9%)	4 (14,3%)	3 (2%)	<b>0,010</b>
• Pericardial	5 (2,8%)	1 (3,6%)	4 (2,6%)	1,000
Pharmacological forms				
• Pharmaco sensitive	838 (97%)	151 (93.2%)	687 (97.9%)	<b>0.001</b>
• Pharmaco resistant	26 (3%)	11 (6.8%)	15 (2.1%)	
Focus				
• Uni focal	669 (77.4%)	98 (60.5%)	571 (81.3%)	<b>&lt;0.001</b>
• Multifocal	195 (22.6%)	64 (39.5%)	131 (18.7%)	

\*: Bacteriologically confirmed pulmonary tuberculosis

\*\*: Clinically diagnosed pulmonary tuberculosis

\*\*\*: Extra pulmonary tuberculosis

## Therapeutic Data of TB-HIV Patients

All the patients screened were immediately put on anti-tuberculosis treatment and 94.8% of the patients had been put on anti-retroviral treatment (ART) (Table 4).

**Table 4:** TB-HIV patient put on ARV treatment.

Year	Total TB-HIV	TB-HIV put on ARV (%)	TB-HIV not started on ART (%)
2018	216	206 (95.4%)	10 (4.6%)
2019	180	173 (96.1%)	7 (3.9%)
2020	140	135 (96.4%)	5 (3.6%)
2021	175	158 (90.3%)	17 (9.7%)
2022	153	147 (96.1%)	6 (3.9%)
Total	<b>864</b>	<b>819 (94.8%)</b>	<b>45 (5.2%)</b>

## Scalable Features

Patients in successful anti-tuberculosis treatment (cured and treatment completed) accounted for 75.1% of cases. The mortality rate was 18.7% (Table 5).

## Mortality Factors

In bivariate analysis, the determining epidemiological factors of TB/HIV patient mortality were children aged 5 to 14 years ( $p < 0.001$ ), female patients ( $p = 0.04$ ), civil servants and patients without occupation ( $p < 0.001$ ). Clinically, tuberculosis, pleural

**Table 5:** Evolutionary characteristics of TB-HIV patients in the Gbêkê region.

	TB-HIV patients	Hit (%)	Failure (%)	Deceased (%)	Lost view	Not evaluated
2018	216	146 (67.6%)	0	59 (27.3%)	11 (5.1%)	0
2019	180	128 (71.1%)	5 (2.8%)	36 (20%)	9 (5%)	2 (1.1%)
2020	140	101 (72.1%)	3 (2.1%)	35 (25%)	1 (0.7%)	0
2021	175	149 (85.1%)	5 (2.8%)	12 (6.9%)	1 (0.6%)	8 (4.6%)
2022	153	125 (81.7%)	4 (2.6%)	20 (13%)	3 (2%)	1 (0.7%)
Total	864	649 (75.1%)	17 (2%)	162 (18.7%)	25 (2.9%)	11 (1.3%)

tuberculosis ( $p=0.04$ ) and meningeal tuberculosis ( $p=0.011$ ) were the determining factors of mortality.

## Discussion

This retrospective study on the aspects of tuberculosis in HIV-infected subjects allowed us to determine the prevalence of HIV in tuberculosis patients and to specify the epidemiological, clinical and evolutionary aspects of tuberculosis in HIV-infected patients in the Gbêkê region in Côte d'Ivoire during the period from January 2018 to December 2022. The limitations of this study were related to its retrospective nature with its corollary of missing data, which could reduce the number of patients. Despite these limitations, the results obtained are reliable and perfectly interpretable.

The prevalence of HIV in tuberculosis patients was 18.7%, this prevalence was 38% in 1998 [7]. It experienced a gradual decline to reach 22.6% in 2018 and has stabilized around 18.5% since 2019. The prevalence of HIV among tuberculosis patients in the Gbêkê region was lower than the national prevalence, which was 24% in 2021 [3]. The drop in HIV prevalence among tuberculosis patients in the region is a reflection of the joint fight led by the PNLT and the PNLs through the creation of several joint screening and care centers for tuberculosis and HIV. In addition, the efforts of actors such as health personnel and community health workers should be mentioned. It must also highlight the availability of new tools for the diagnosis of tuberculosis (molecular biology, geneXpert) and therapeutic progress in the management of HIV and the prevention of tuberculosis in patients living with HIV (prophylaxis by isoniazid) [3,5]. However, this prevalence remains high all the same and testifies to the late discovery of HIV infection in countries with limited resources [9,10]. The average age of the patients was 37 years old. The youth of the population reflects the age pyramid of our country [8]. Our results are consistent with findings from studies conducted in countries with high TB and HIV endemicity in Africa [9-11]. Patients in the 25 to 49 age group were in the majority. Indeed, this age group constitutes the most professionally active population and their illness constitutes a brake on the economic development of underdeveloped countries in Africa [12]. At the family level, the impact is all the greater since the sick person is the main financial support of the family (head of the family). The female predominance observed in our study was found by several authors in previous studies in Bouaké and in other African countries [13]. Also, women are more exposed to HIV in Africa because of certain social constraints such as forced marriage, excision, polygamy and also anatomical predispositions (wider exposure surface) [13]. The fear of stigmatization in society forces these women to hide their

HIV status, consequently these women are poorly monitored and exposed to all opportunistic diseases including tuberculosis [9]. In addition, these women, most often without financial income, are dependent on men, thus favoring the late discovery of their illnesses at the stage of opportunistic infections [13]. Healthcare workers accounted for 2.6% of infected patients. This staff could be infected in the exercise of their function when they do not respect individual protection measures. These measures are not always respected by staff either through negligence, ignorance or lack of protective equipment [14]. It is therefore necessary to train healthcare personnel in the use of protective equipment and to equip health centers with personal protective equipment.

The pulmonary form of tuberculosis (79.3%) was the most observed in HIV-infected patients, with a predominance of clinically diagnosed and miliary forms. This testifies to the difficulty of diagnosing cases of tuberculosis in our low-income countries [16]. Indeed, the majority of centers only have microscopy for the diagnosis of tuberculosis, molecular biology devices (geneXpert) being available only at the anti-tuberculosis center of Bouaké. The diagnosis of tuberculosis therefore rested in the event of a negative microscopic smear on and radiological arguments explaining the high frequency of TPB-. The extra-pulmonary forms dominated by pleural and lymph node tuberculosis also occupied an important place in the cases of tuberculosis in HIV-infected subjects. The predominance of the pulmonary form had also been found by Horo et al. in Abidjan [9]. Contrary to our study, some authors observed a predominance of the extra-pulmonary form in HIV-infected patients [7]. However, these studies had been carried out before the advent of the involvement of molecular biology in the diagnosis of tuberculosis and in these studies, miliary tuberculosis was considered as an extra pulmonary form [15]. Multiple infectious foci were frequent, testifying to the depth of immunosuppression during the diagnosis of tuberculosis [9,11]. Patients consult the centers only as a last resort after self-medication and traditional treatment [13]. There is also the denial of the disease and the fear of rejection and stigmatization, which are at the origin of the delay in consultation and the extension of tuberculosis to several organs [13]. All patients who had a positive sputum examination and those in whom there was a strong suspicion of tuberculosis were immediately started on anti-tuberculosis treatment. This treatment was supervised by a community counselor and a close relative throughout the duration of the medication intake in accordance with the recommendations of the PNLT [3]. As for antiretroviral treatment only, 94.8% had received this treatment. This rate was very close to the objectives set by the WHO, which was 95%. Efforts are still needed to improve this rate of treatment in the

region. Patients who had not been put on ARV treatment were lost to sight and had been diagnosed in centers that did not provide HIV treatment. It is therefore essential to extend the integrated management of HIV and tuberculosis in all tuberculosis diagnostic centers in Côte d'Ivoire. Similar results were found in data from several countries with high HIV and TB endemicity in Africa [11,12].

In evolutionary terms, the mortality of TB/HIV was high (18.7%). Late detection of HIV infection is one of the most common causes of mortality in all countries with high endemicity of both diseases [7,17]. The factors related to mortality in our study were the age group from 5 to 14 years ( $p < 0.001$ ), female patients ( $p = 0.04$ ), civil servants and patients without profession ( $p < 0.001$ ), pleural tuberculosis ( $p = 0.04$ ), meningeal tuberculosis ( $p = 0.011$ ). These results were also found in several other studies [7,9,17].

## Conclusion

This retrospective study allowed us to take stock of current aspects of tuberculosis in HIV-infected subjects in the health region of Gbêkê in Côte d'Ivoire. Analysis of the results showed that HIV prevalence among TB patients was decreasing but remained high despite the efforts of national HIV and TB control programs. The co-infected patients were generally young female adults living in a couple. The pulmonary form of tuberculosis was predominant and pleural tuberculosis was the most frequent extra-pulmonary form. Mortality was high and was related to the age group of 5 to 14 years, female gender, civil servants, unemployed patients and pleural and meningeal forms of tuberculosis. Joint efforts by the PNLs and the PNLT are still needed to eradicate TB/HIV co-infection.

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