

# Extrapulmonary Tuberculosis: Prevalence and Associated Factors in the Infectious Diseases Department of the Brazzaville University Hospital

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**Abstract Objective:** Determine the prevalence of extra-pulmonary tuberculosis in the Infectious diseases department of the University Hospital of Brazzaville and look for associated factors. **Patients and method:** Cross-sectional study aimed at descriptive and analytical description of cases of extra-pulmonary tuberculosis hospitalized in the infectious diseases department between 1<sup>st</sup> January 2019 and June 30, 2021 (30 months) in patients infected with HIV or not, receiving treatment or not highly active antiretroviral drug and who gave free and informed consent to participate in this study. **Results:** A total of 100 hospitalized patients (5.4% of admissions) mean age  $44.05 \pm 12.7$  years [18-76], female (55%) had a secondary education level (n=53; 53%), single (n=79; 79%), lived in town (93%) and infected with HIV (92.6%). The average consultation time was  $41.6 \pm 10.5$  [1-210] days, mainly for fever (85%) and impaired general condition (63%). Tuberculosis was localized in the lymph nodes and lungs (29%), pleural (22%) and lymph nodes alone (17%). The various opportunistic infections found were CNM (n=12), cerebral toxoplasmosis (n=9). The Mean CD4 counts were  $165.2 \pm 56.8$  [2-644]. IDRT was anergic in 68.4% and GenXpert was positive in 23% of cases. Abdominal ultrasound found ADP (38%) and ascites (13%). EHRZ treatment was administered in 81% of cases and ART introduced within an average of  $30.9 \pm 7.7$  days. It was mainly from the TDF+FTC+EFV combination in 36% of cases. The mean hospital stay was  $17.8 \pm 14$  [1-90] days. The overall lethality was 51% (n=51) due to anemic shock (n=17; 33.3%) and septic (n=12; 23.5%). Age (p=0.03), being single (p=0.02), meningeal syndrome (p=0.006) and coma (p=0.02) were related to the occurrence of death. **Conclusion:** The hospital prevalence of tuberculosis extrapulmonary is high in the infectious diseases department of the CHUB as is the lethality, despite early treatment. Age and neurological location influence the prognosis, which is to say the importance of prevention.

**Keywords:** tuberculosis, extra pulmonary, prevalence, CHU-Brazzaville

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## 1. Introduction

Extra-pulmonary tuberculosis reflects the localization of *Mycobacterium tuberculosis* outside the granuloma, either hematogenously (disseminated tuberculosis or miliary tubercleuse) or via the lymphatic route (nodal tuberculosis). It remains a real public health problem in sub-Saharan Africa, responsible for high morbidity and mortality, often linked to HIV/AIDS infection [1]. The diagnosis extrapulmonary forms is often made difficult not only because of the very deep localization of the

KOCH bacillus but also because of the weakness of the technical platform in the context of countries with limited resources [2].

In the Congo, most of the studies carried out on tuberculosis in the hospital environment concern its main pulmonary localization and few studies at the Brazzaville University Hospital have addressed the problem of the extra bronchial localization of BK, hence the purpose of this work which had as a goal determination of the prevalence of extra-pulmonary tuberculosis in the infectious diseases department of the CHUB, including the identification of associated factors.

## 2. Patients and Method

This was a cross-sectional study aimed descriptive and analysis of cases of extra-pulmonary tuberculosis hospitalized in the infectious diseases department between 1<sup>st</sup> January 2019 and June 30, 2021, i.e. 30 months. Patients with or without HIV infection, receiving or not receiving high-level antiretroviral therapy active and having given a free and informed consent to participate in this study was included. The epidemiological variables (age, sex, level of education, marital status, HIV status as well as the notion of previous tuberculosis), clinical (Reason and time for consultation) diagnostic (topographic forms of tuberculosis, diagnostic procedures), therapeutic (time to start EHRZ-ARV treatment) and evolutionary (Duration of hospitalization, cure, relapses, deaths and causes of death) were studied.

The data was collected using a pre-designed survey form, and analyzed using the EPI software. Info 3.3.1 with the determination of qualitative and quantitative variables from statistical tests according to their applicability criteria. For all the tests used, the significance threshold was set at <0.05.

## 3. Operational Definitions

The diagnosis of Extra pulmonary tuberculosis (EPT) was evoked and retained according to a range of epidemiological arguments, clinical, diagnostic and/or therapeutic (retrospective diagnosis after completion of a trial treatment).

Case of extra pulmonary Tb: all bacteriologically confirmed case or a clinically diagnosed case of Tb involving organs other than the lungs (pleura, lymph node, abdomen, genitourinary, tract, skin, joints and bones, meninges).

## 4. Results

Of all the cases of tuberculosis, 32.3% of EPT were found, while in the whole of the study population, there were found one hundred (100) hospitalized patients (5.4% of admissions) average age of  $44.05 \pm 12.7$  years [18-76], female (55%) and male (45%), with secondary education (n=53; 53%), single (n=79; 79%), employed (43%) and comerchants (27%). They lived in town (93%) and infected with HIV (92.6%) with a low socioeconomic level (71%). HIV infection was discovered during hospitalization (n=75; 92.6%). The average consultation time was  $41.6 \pm 10.5$  [1-210] days, mainly for fever (85%) and poor general condition (63%). These were new cases (66%) and relapses (13%). Tuberculosis was located in the lymph nodes and lungs (29%), pleural (22%) and lymph nodes alone (17%) (Figure 1). The various opportunistic infections found were CNM (n=12), cerebral toxoplasmosis (n=9). Mean CD4 counts were  $165.2 \pm 56.8$  [2-644]. IDRT was anergic in 68.4% and GenXpert in the casing liquid gastric was positive in 23% of cases. Abdominal ultrasound found ADP (38%) and ascites (13%) (Figure 2) while the chest X-ray objective iodopacity occupying the entire hemithorax erasing the ipsilateral dome, with a repression of the mediastinum testifying to a pleurisy of great abundance (Figure 3). EHRZ treatment was administered in 81% of cases and ART introduced within an average of  $30.9 \pm 7.7$  days. It was principal payment of the TDF+FTC+EFV association in 36% of cases. The mean hospital stay was  $17.8 \pm 14$  [1-90] days. The overall lethality was 51% (n=51) due to anemic shock (n=17; 33.3%) and septic shock (n=12; 23.5%). Age (p=0.03), single being (p=0.02), meningeal syndrome (p=0.006) and coma (p=0.02) were related to the occurrence of death (Table 1).

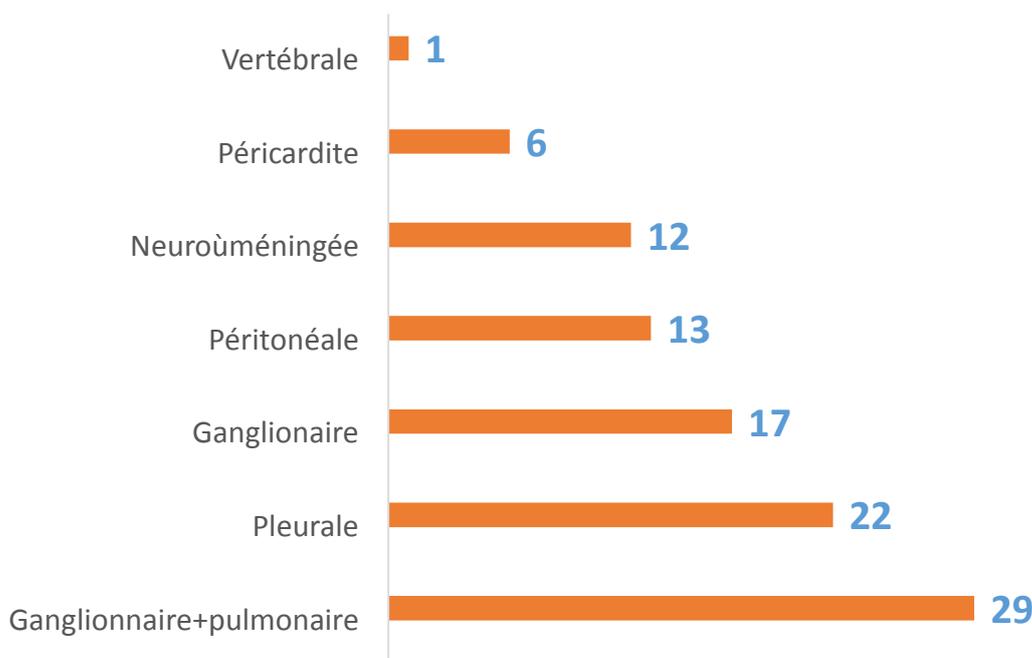
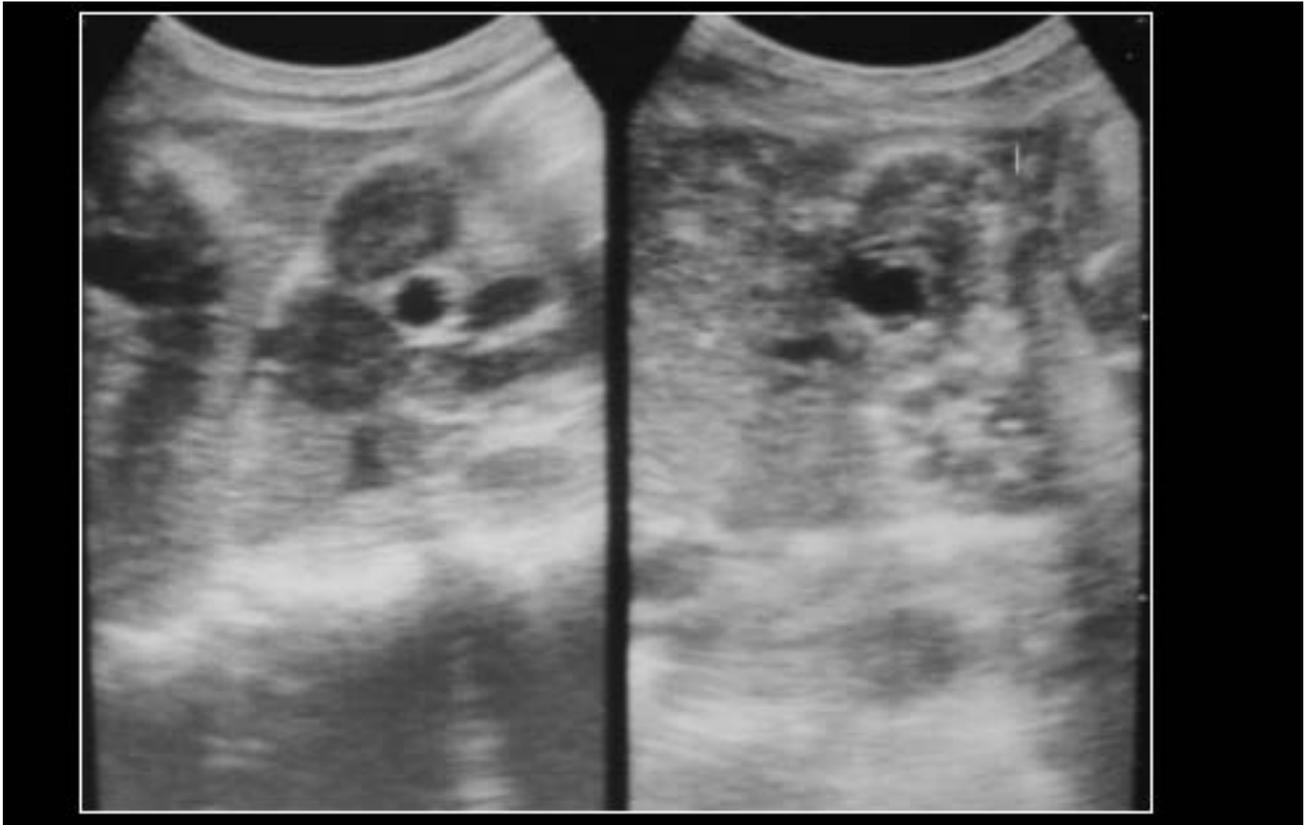
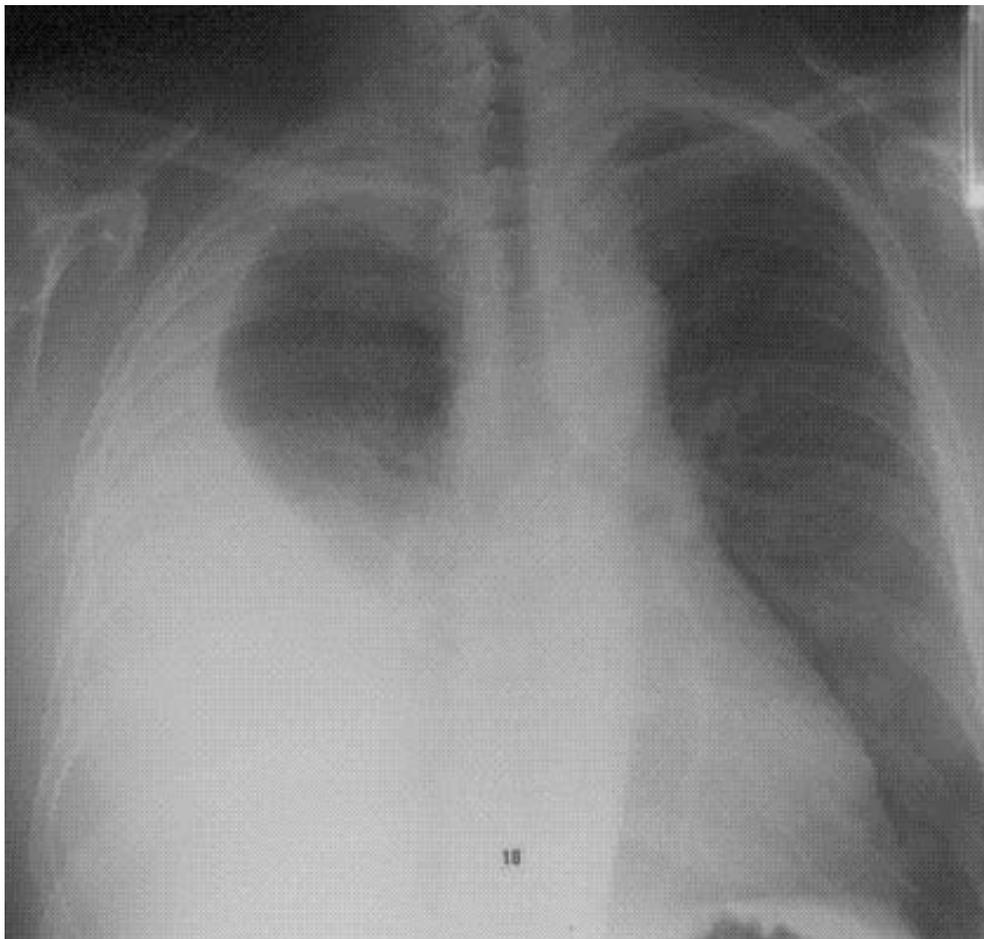


Figure 1. Different clinical forms of PET



**Figure 2.** Hypoechoic mesenteric lymphadenopathy related to digestive tuberculosis



**Figure 3.** Frontal Chest X-ray (Pleurisy)

Table 1. Associated factors

Associated factors	EVOLUTION				GOLD	95% CI	p value
	Death (n=51)		Cured (n=47)				
	Workforce	Percentage	Workforce	Percentage			
<b>age range</b>							
<20 years	0	0.0	4	8.5	0.0		<b>0.03</b>
<b>Marital status</b>							
Single	36	70.6	42	89.4	0.2	0.09-0.8	<b>0.02</b>
<b>Reason for hospitalisation</b>							
Diarrhea	12	23.5	2	4.3	6.9	1.4-32.8	<b>0.006</b>
<b>Examination signs</b>							
Coma	24	47.1	12	25.5	2.5	1.1-6.1	<b>0.02</b>
Neck stiffness	12	23.5	4	8.5	3.3	1.09-11.1	<b>0.04</b>
Kerning sign	10	19.6	1	2.1	11.2	1.3-91.4	<b>0.006</b>
Brudzinski's sign	9	17.6	1	2.1	9.8	1.1-81.1	<b>0.01</b>
<b>EHRZ treatment</b>	37	72.5	44	93.6	0.1	0.04-0.6	<b>0.006</b>
<b>GenXpert</b>							
Positive	4	16.0	18	51.4	0.1	0.05-0.6	<b>0.004</b>
Negative	21	84.0	17	48.6	5.5	1.5-19.5	<b>0.004</b>

## 5. Discussion

Our study has some biases related to its partly retrospective nature. Some information does not have could not be found in medical records and hospital registers. In addition, the weakness of the technical platform did not make it possible to confirm the diagnosis of extra-pulmonary tuberculosis in certain cases. All these difficulties have already been encountered by most African authors [2,3] However, this study has lifted the veil on the situation of extra-pulmonary tuberculosis at the Brazzaville University Hospital.

The prevalence of cases of extra-pulmonary tuberculosis is high in the infectious diseases department of the Brazzaville University Hospital compared to that reported in some countries of the sub-region [2,3,4]. Extra-pulmonary and disseminated forms of tuberculosis interest 56.2% of patients in Madagascar, whereas they accounted for 53% of tuberculosis cases in Nairobi and 57% in North Carolina [5,6].

The average age of patients with extra-pulmonary tuberculosis was 44 years and the age group between 30 and 49 years was the most represented. This is a category of the most active population, living in conditions of promiscuity. These are mostly female patients in connection with the feminization of HIV infection. These data are consistent with those reported in the African literature [4,7].

The unemployed represented the category of the population most affected, followed by traders. Our study finds a proportion of 43% of patients with tuberculosis who do not have a job. This result suggests that poverty influences on tuberculosis whatever the clinical form in sub-Saharan Africa [1,8].

Singles were the most represented social stratum in 79% of cases. Almost all of these patients resided in the city. These are agglomerations high population density, favorable to the transmission of *mycobacterium tuberculosis* as reported in the literature [2,3,9]. In the vast majority of cases, HIV1 infection was discovered during hospitalization. Tuberculosis remains one of our days the first opportunistic infection in the subject infected with HIV and this association is not a new fact since it has

already been observed in several African series [1,3,9,10,11]. The average consultation time was 41.6 days with extremes ranging from 1 to 210 days. These long delays in consultation are classic in African settings [3,5,7]. Indeed, the denial of the disease specific to the populations studied and the low socio-economic level largely justify this delay in consultation insofar as patients sometimes consult above all traditionally before resorting to a health structure only belatedly. Meningeal syndrome in a context of psychomotor agitation, signs of neurological deficit hemiplegia and as cited were the most common physical examination signs in patients.

Lymph node and pulmonary tuberculosis followed by pleural localization were the main clinical forms encountered in patients and in 29% of cases, the lymph node form was associated with pulmonary localization. In accordance with data from the literature, lymph node involvement was more observed, associated with pulmonary localization in patients immunocompromised by HIV without statistically significant difference ( $p=0.1$ ) [11,12]. In Madagascar, in a hospital environment, peripheral lymph node involvement was the most represented form in 53.1%, followed by osteo-articular forms as reported by Ralisata and collaborators [5].

Neuromeningeal cryptococcosis and cerebral toxoplasmosis were the main opportunistic infections associated with extra pulmonary tuberculosis in patients. Advanced immunosuppression has as its corollary the appearance of these opportunistic infections which must always be systematically sought in any HIV-positive patient presenting with a PET scan.

The intradermal reaction to tuberculin came back negative in 68.4% of cases. It was more negative in patients immunocompromised by HIV versus immunocompetent patients. In Dakar in a series of pleural tuberculosis in 2010, this rate was 42.5%. These rates were higher than that reported in Spain by Valdés [8]. In Senegal, the negativity rate was 65.4% in HIV-positive patients versus 29% in HIV-negative patients. These results are explained by the decrease in cellular immunity at the origin of anergy in patients living with HIV. The tuberculin skin test therefore has no interest in severely immunocompromised individuals. During

tuberculosis, normocytic anemia is most often reported. We found an average hemoglobin level of 7.4g/dl. This often inflammatory anemia is usually described during tuberculosis-HIV co-infection thus making the prognosis unfortunate as already reported in Congo and Mali [7]. GeneXpert in the pathological product was performed in 61 patients and came back positive in 23% of cases. In no case was pathogen resistance to rifampicin detected. The sensitivity and specificity of GeneXpert in the diagnosis of pulmonary and extra-pulmonary tuberculosis have been evaluated in several studies with nevertheless variable results [13,14]. However, in 38% of cases a negative result was noted. This variation in the sensitivity and specificity of the GeneXpert test depending on the type of sample could be explained by the fact that the mycobacterial load, which varies according to the different compartments of the body, is the main determinant of the positivity of the test. When abdominal ultrasound was available, deep para-aortic or coeliomesenteric lymphadenopathy was found in 28 cases. Peritoneal tuberculosis was found in 17 patients. This diagnosis had been suspected by the cyto-biochemical analysis of the exudative liquid of ascites and confirmed by the results of the therapeutic trial. The contribution of ultrasound in the diagnosis of tuberculosis peritoneal as it is recognized in the African context [15]. Laparoscopy with demonstration of peritoneal granulomas constituting the most common endoscopic sign was not performed in our study. The treatment of tuberculosis in our patients obeyed the recommendations issued by the WHO and the national tuberculosis control program of Congo [1,16] in 81% of cases. In negligible proportions, anti-tuberculosis treatment was not instituted, this in connection with the rapid and fatal progression observed in some patients. The overall lethality was 51%, high compared to that seen elsewhere. Age less than 20 years, being single and neurological localization had a statistical link significantly with the occurrence of death in patients.

The low standard of living of patients for whom the cost of co-infection management is out of reach, delayed diagnosis, advanced immunosuppression, working conditions characterized by limitation of diagnostic and therapeutic means would largely explain this high mortality rate found.

## 6. Conclusion

The prevalence of EPT in the infectious diseases department at the Brazzaville University Hospital is high, as is the lethality. Mostly found in HIV-positive, lymph node localization predominated and the associated factors remain age and neurological localization. The prevention of this condition remains the only cost-effective measure and involves raising the socio-economic level of populations, screening and early management of HIV infection.

## Conflict of Interest

The authors emphasize that they have no conflict of interest in relation to this study.

## Abbreviation

ADP: Lymphadenopathy  
 EPT: Extrapulmonary tuberculosis  
 IDRT: Intradermal tuberculin reaction  
 CNM: Neuromeningeal cryptococcosis

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