

EXTRAPULMONARY TUBERCULOSIS AT THE SYLVANUS OLYMPIO UNIVERSITY HOSPITAL CENTER

Abstract

Objective: describe the epidemiological, clinical, paraclinical and therapeutic aspect of extrapulmonary tuberculosis at centre hospitalier universitaire Sylvanus Olympio in Lomé.

Methodology: This was a retrospective and descriptive study over a period of 2 years, from November 2020 to October 2022, of extrapulmonary tuberculosis cases diagnosed at CHUSO in Lomé, and put on treatment.

Results: We identified 66 cases of extrapulmonary tuberculosis during this period. The average of age of patients was 43.39 years old, with the extreme of 4 and 85 years. Low socioeconomic level was found on 65.2 % of patients. An history of tuberculosis contamination was found on 4.6% of patients. On the 66 patients of our study, 31 performed BCG vaccination. An HIV infection was found on 21.2 %. In our study, loss of weight was found on 47 patients and 30 patients had vesperal fever. In our study the main localization was osteoarticular with 53.0 %. The diagnosis was presumptive in 78.8 % of cases. A confirmation diagnosis was most often histological (12.1%). All our patients received a standard antituberculosis treatment, RHEZ during the initial phase. We noticed 3.0 % of death with a significative association with HIV infection.

Conclusion: Extrapulmonary tuberculosis concerns all groups of age. Immunodepression favors its development. Its diagnosis is most often presumptive.

Keywords: Pott's disease, HIV, diagnosis tools, Lomé (Togo).

INTRODUCTION

Tuberculosis remains a major public health concern throughout the world and particularly in sub-Saharan Africa. According to the World Health Organization (WHO), the prevalence of latent tuberculosis infection worldwide is estimated at 1.7 billion, or approximately a quarter of the world's population [1]. Despite the decline in the incidence of this disease, the WHO estimates around 9.9 million new cases of tuberculosis in 2020, with around 1.5 million deaths per year [2, 3]. Africa alone records nearly a quarter of the global incidence, especially in countries with a high burden of human immunodeficiency virus (HIV) infection.

In Togo, although the incidence of tuberculosis follows the global trend, this disease remains relevant and still poses a public health problem.

The diagnosis of tuberculosis is primarily bacteriological and requires a specific bacteriological examination with a culture on a particular medium. In certain cases, a histological study finding the tuberculous granuloma allows the diagnosis to be made. Molecular biology techniques are increasingly used, making it possible not only to reveal the genetic material of the mycobacteria but also to detect the mutations responsible for bacterial resistance [4].

Although the pulmonary form is predominant, the extrapulmonary forms are more complex and pose a management problem. Bacteriological documentation is more difficult, histological examination is a great aid to diagnosis. In these extrapulmonary forms the diagnosis is often presumptive using anamnestic, clinical, biological, morphological and histological arguments [5].

However, genetic amplification techniques have improved the diagnosis of extrapulmonary tuberculosis [6]. In terms of treatment, the duration is in certain cases prolonged, particularly in the osteoarticular and neuromeningeal forms. HIV infection, through the immunosuppression it causes, promotes the occurrence of extrapulmonary forms of tuberculosis. The risk is higher in patients not treated with antiretrovirals.

Extrapulmonary tuberculosis accounts for approximately 20-40% of tuberculosis cases worldwide. It is described in the literature as being more common in immunocompromised patients and black subjects [5].

To our knowledge, few studies have focused on extrapulmonary tuberculosis [7, 8]. It seemed important to us to undertake this study, the general objective of which was to identify the most frequent forms of extrapulmonary tuberculosis in our hospital context.

Our specific objectives are to describe the epidemiological, clinical, paraclinical, therapeutic and progressive aspects of extrapulmonary tuberculosis seen at the Sylvanus Olympio university hospital center in Lomé.

STUDY FRAMEWORK AND METHOD

STUDY FRAMEWORK

The Sylvanus Olympio University Hospital Center (CHU SO) served as the setting for our study. It has a capacity of 1264 beds. It has 5 specialty groups: surgery and surgical specialties, pediatrics, gynecology and obstetrics, medicine and medical specialties, clinical biology.

There are 2 groups of practitioners: university hospitals and hospitalists. It receives an average of 101,350 patients per year. Around 20,130 patients are hospitalized each year. The implementation of information and communication technology methods is still in its infancy and the archiving of files is classic.

STUDY METHOD

TYPE AND PERIOD OF STUDY

This was a descriptive study with retrospective data collection, which took place over a period of 2 years, from November 1, 2020 to October 31, 2022.

STUDY POPULATION

The population consisted of patients hospitalized in one of the departments of the CHU SO with a definite or presumptive diagnosis of extrapulmonary tuberculosis and placed on anti-tuberculosis treatment.

The definitive diagnosis of tuberculosis was:

- either histological, by the demonstration of tuberculous granuloma made up of epithelioid cells and giant cells with caseous necrosis,

- either bacteriological, by the demonstration of AFB on direct examination and the identification of a strain of tuberculous mycobacteria on culture,
- or Molecular, by the detection of the bacterial genome using the GeneXpert MTB/RIF test.
- The presumptive diagnosis was based on the practitioner's judgment based on sociodemographic, anamnestic, clinical, biological and morphological arguments.

INCLUSION CRITERIA

All patients with a definite or presumptive diagnosis of extrapulmonary tuberculosis established at the SO University Hospital and placed on anti-tuberculosis treatment during the study period were included.

NON-INCLUSION CRITERIA:

Not included in the study were patients with a diagnosis of extrapulmonary tuberculosis whose files were incomplete and unusable.

DATA COLLECTION

Data collection consisted of analyzing patient files, department by department, using a pre-established survey form. The following variables were taken from patient files and studied: epidemiological variables, socioeconomic level, clinical variables (main reason for admission, consultation delay, tuberculosis infection, BCG vaccination, comorbidities, signs of tuberculosis impregnation), paraclinical variables (IDR to tuberculin, search for AFB, and GeneXpert in sputum, biological fluids (ascites puncture fluid, pleural, pericardial, ear discharge), histology of biopsy specimens (nodal, appendicular, osteoarticular), histology of biopsy specimens), therapeutic and evolving variables (anti-tuberculosis therapeutic regimen, adjuvant corticosteroid therapy, hospital evolution).

ETHICAL CONSIDERATION

The data was analyzed anonymously.

DATA ANALYSIS

The collected data were entered into a Microsoft® Excel 2021 file. The resulting database was exported into STATA® version 15 for processing and analysis. The calculation of the p value was done using the chi-square formula according to the observed value and the expected value in

order to know the significant correlations. This calculation was performed automatically using SPSS version 3.0 software. The graphs were created using Microsoft® Excel 2021.

OPERATIONAL DEFINITION

➤ Socioeconomic level (NSE)

It was subdivided into 3 groups based on the patients' assumed income:

- High NSE if the income is estimated to be greater than 250 euros or 150,000 CFA francs per month,
- Average NSE if income is estimated between 52 euros and 250 euros, or between 35,000 and 150,000 CFA francs per month,
- Low NSE if income is estimated less than or equal to 52 euros or 35,000 CFA francs per month corresponding to the SMIG.

- Consultation time: time elapsed between the date of appearance of the first symptoms and the date of consultation.
- Nosocomial infection: infection occurring during the hospital stay.
- Hospital evolution: evolution during the patient's stay in hospital.
- Favorable evolution: clinical and/or paraclinical improvement after initiation of anti-tuberculosis treatment.

	Effective	Percentage
Spinal pain	60	45.5
Chest pain	28	21.2
Dyspnea	16	12.1

RESULTS

EPIDEMIOLOGICAL ASPECTS

The hospital frequency was 132 cases over 4 years of extrapulmonary tuberculosis.

The average age was 42.39 years, with extremes of 4 and 85 years. The most common age group was 40 to 60 years old, or 34.85% of cases.

We recorded 64 men (48.48%) and 68 women (51.52%), giving a M/F sex ratio of 0.94.

CLINICAL ASPECTS

Reason for consultation and history

Spinal pain was the main reason for consultation in 45.5% of cases (Table I).

Table I: Distribution of patients according to reason for consultation

Abdominal pain	8	6.1
Fever	6	4.6
Polyadenopathy	4	3.0
Groin pain	2	1.5
Generalized edema	2	1.5
Oligoarthritis	2	1.5
Paraparesis	2	1.5
Eardischarge	2	1.5

The average consultation time was 119.12 days with extremes of 14 days and 720 days. The notion of tuberculosis infection was found in 6 patients (4.6%). Thirty-one patients, or 47.0% of patients, had received BCG vaccination. The BCG vaccination status of the other patients was unknown. HIV infection was found in 28 patients, or 21.2% of cases (table II).

Table II: distribution of patients according to comorbidity and lifestyle

	Effective	Percentage
HIV infection	14	21.2
Alcohol consumption	12	18.2
Smoking	6	9.1
Diabetes	3	4.6
Hypertension	3	4.6
Viral hepatitis B	1	1.5
IRC	1	1.5

Hypertension: high blood pressure. HIV: human immunodeficiency virus. CKD: chronic renal failure.

SIGNS OF TUBERCULOUS IMPREGNATION

One hundred and sixteen patients, or 87.9% of patients, presented at least one sign of tuberculosis impregnation. Weight loss was present in 94 patients, or 71.2% of cases (Figure 1).

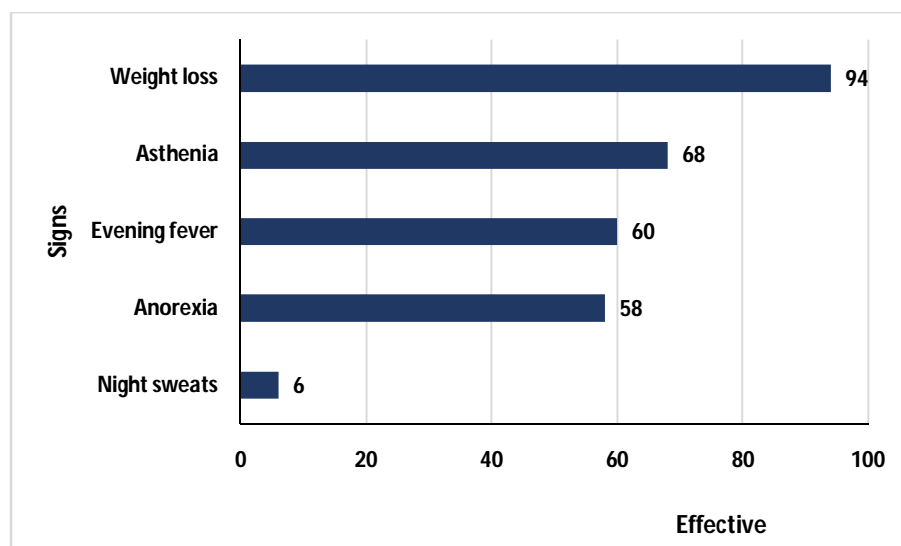


Fig 1: distribution of patients according to the frequency of signs of tuberculosis impregnation

DIAGNOSTIC METHOD

The diagnosis was presumptive in 104 cases (78.8%) (Table III).

	Effective	Percentage
Histology	16	12.1
Molecular (GeneXpert)	10	7.6
Bacteriology	2	1.5
Presumption	104	78.8
Total	132	100

Of the 35 cases of osteoarticular tuberculosis, 34 cases had a presumptive diagnosis and 1 case had a definite diagnosis, i.e. 97.1% and 2.9% of cases respectively (Table IV).

Table IV: Distribution of patients according to location of tuberculosis and type of diagnosis

	Diagnosis	Diagnosis of	Total
	presumptive	certainty	
	n (%)	n (%)	n (%)
Osteoarticular tuberculosis	68 (97.1)	2(2.9)	70 (100.0)
Pott's disease	64 (97.0)	2 (3.0)	66 (100.0)
Coxalgia	2 (100.0)	0 (0.0)	2 (100.0)
Sacroileitis	2 (100.0)	0 (0.0)	2 (100.0)
Pleural tuberculosis	14 (50.0)	14 (50.0)	28 (100.0)
Digestive tuberculosis	8 (80.0)	2 (20.0)	10 (100.0)
Peritoneal tuberculosis	8 (100.0)	0 (0.0)	8 (100.0)
Appendicular tuberculosis	0 (0.0)	2 (100.0)	2 (100.0)
Pericardial tuberculosis	4 (50.0)	4 (50.0)	8(100.0)
Lymph node tuberculosis	0 (0.0)	8 (100.0)	8 (100.0)
Atrial tuberculosis	0 (0.0)	2 (100.0)	2 (100.0)
Multifocal tuberculosis	10 (100.0)	0 (0.0)	10 (100.0)
Tuberculous polyseritis	10 (100.0)	0 (0.0)	10(100.0)
Total	104 (78.8)	28 (21.2)	132 (100.0)

MEANS OF CERTAINTY DIAGNOSIS

Ten (10) cases of tuberculosis were confirmed by molecular biology. Resistance to rifampicin was not found (table V).

Table V: distribution of patients according to the location of tuberculosis and the means of definitive diagnosis

	Biologiemoléculaire	Bactériologie	Histologie	Total
	n(%)	n(%)	n(%)	n(%)

Osteoarticular tuberculosis	0 (0.0)	0 (0.0)	2 (100.0)	2 (100.0)
Pleural tuberculosis	4(28.6)	2(14.3)	8(57.1)	14(100.0)
Lymph node tuberculosis	0(0.0)	0(0.0)	4(100.0)	4(100.0)
Pericardial tuberculosis	2(100.0)	0(0.0)	0 (0.0)	2(100.0)
Digestive tuberculosis	0 (0.0)	0 (0.0)	2 (100.0)	2 (100.0)
Atrial tuberculosis	2 (100.0)	0 (0.0)	0 (0.0)	2 (100.0)
Total	10 (35.8)	2 (7.1)	16 (57.1)	28 (100.0)

LOCATION OF TUBERCULOSIS AND COMORBIDITES

Twenty-eight (28) tuberculosis patients, including 10 with osteoarticular localization, had HIV infection (table VI).

Table VI: distribution of patients according to the location of the tuberculosis and main Alcoholconsumption

	HIV infection	comorbidities and lifestyle	Smoking	Diabetes
	n	n	n	n
Osteoarticular	10	10	6	4
Pleural	6	6	4	2
Digestive	6	2	2	0
Pericardial	0	1	0	0
Ganglionic	4	0	0	0
Auricular	2	0	0	0
Multifocal	0	4	0	0
Total	28	24	12	6

THERAPEUTIC AND EVOLUTIONAL ASPECTS

ANTI-TUBERCULOSIS DIET

All patients were new cases and received in the initial phase a regimen consisting of a combination of 4 first-line anti-tuberculosis drugs: rifampicin, isoniazid, pyrazinamide and ethambutol (RHZE), prescribed for a period of 2 months, then at continuation phase dual therapy based on rifampicin and isoniazid.

ADJUVANT CORTICOTHERAPY

In addition to anti-tuberculosis treatment, 58 patients or 44% of cases had received adjuvant corticosteroid therapy (Table VII).

Table VII: distribution of patients according to the location of tuberculosis and the administration of adjuvant corticosteroid therapy

	Corticotherapy		
	Yes n(%)	No n(%)	Total n(%)
Osteoarticular tuberculosis	40 (57.1)	30 (42.9)	70(100.0)
Pott's disease	40 (60.6)	26(39.4)	66(100.0)
Coxalgia	0 (0.0)	2(100.0)	2 (100.0)
Sacroileitis	0 (0.0)	2(100.0)	2 (100.0)
Digestive tuberculosis	0 (0.0)	10(100.0)	10(100.0)
Pericardial tuberculosis	8(100.0)	0(0.0)	8(100.0)
Pleural tuberculosis	0(0.0)	28(100.0)	28(100.0)
Lymph node tuberculosis	0 (0.0)	4 (100.0)	4 (100.0)
Atrial tuberculosis	0 (0.0)	2(100.0)	2 (100.0)
Multifocal tuberculosis	10(100.0)	0(0.0)	10(100.0)
Total	58 (44.0)	74 (56.0)	132(100.0)

EVOLUTION

The hospital outcome was favorable in 128 patients (97%) and marked by death in 4 patients (3%).

The 4 deaths occurred during the first month of treatment, one in a picture of immune restoration syndrome and the other secondary to an undocumented probable nosocomial infection.

The low NSE did not seem to influence the evolution (Table VIII).

Table VIII: Evolution according to socio-economic level

	Favorable development	Deaths	Total
	n(%)	n(%)	n(%)
Low NSE	82(95.3)	4(4.7)	86(100.0)
NSE Medium	38(100.0)	0 (0.0)	38(100.0)
NSE High	8(100.0)	0(0.0)	8 (100.0)
Total	128 (97.0)	4 (3.0)	132(100.0)

P=.0576

There was an association between progression and HIV infection with a $P=.008$ (table IX).

Tableau IX: evolution of patients according to comorbidity

	Evolution						p
	Favorable		Deaths		Total		
	n	(%)	n	(%)	n	(%)	
HIV							.0008
Yes	26	(86.7)	4	(13.3)	30	(100.0)	
No	102	(100.0)	0	(0.0)	102	(100.0)	
Total	128	(97.0)	4	(3.0)	132	(100.0)	
Diabetes							.0754
Yes	6	(100.0)	0	(0.0)	6	(100.0)	
No	122	(96.8)	4	(3.2)	126	(100.0)	
Total	124	(97.0)	4	(3.0)	132	(100.0)	
Alcohol							.0800
Yes	24	(100.0)	0	(0.0)	24	(100.0)	
No	104	(96.3)	4	(3.7)	108	(100.0)	
Total	128	(97.0)	4	(3.0)	132	(100.0)	
Smoking							.0650
Yes	12	(100.0)	0	(0.0)	12	(100.0)	
No	116	(96.7)	4	(3.3)	120	(100.0)	
Total	128	(97.0)	4	(3.0)	132	(100.0)	
HTA							.0754
Yes	6	(100.0)	0	(0.0)	6	(100.0)	
No	122	(96.8)	4	(3.2)	126	(100.0)	

Total	128	(97.0)	4	(3.0)	132	(100.0)
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DISCUSSION

STRENGTH AND LIMITATIONS OF THE STUDY

Our study, carried out at the Sylvanus OLYMPIO University Hospital which is the national reference center in Togo, allowed us to take stock of extrapulmonary tuberculosis, particularly the difficulty in the diagnostic and therapeutic approach. The retrospective nature is an important limitation, making it impossible to gather all the essential data required. During the study period from November 2020 to October 2022, the world experienced a health crisis related to Covid-19 infection, which reduced hospital attendance and reporting of tuberculosis cases, thus possibly explaining our low sampling. This study has the advantage and importance of showing the public authorities and health authorities the persistence of tuberculosis in the population in all clinical forms. Particular emphasis must be placed on the systematic detection and treatment of all cases of tuberculosis.

DIAGNOSTIC ASPECTS

CONSULTATION DEADLINE

In our study, we found an average consultation time of 119.12 days. Hamrouni et al. in Tunisia, found an average consultation time of 240 days [9]. Loubna in Morocco found a processing time of 45 days [10]. This long consultation period can be explained on the one hand by the slow and insidious progression of tuberculosis and on the other hand by the insufficient health education of populations in developing countries who preferred to try traditional herbal medicine before any consultation in a hospital environment.

HISTORY AND COMORBIDITIES

Only 6 of our patients, or 4.6% of patients, declared a notion of tuberculosis contagion. Loubna found 32.5% tuberculosis contagion [10]. The retrospective nature of our study may explain this difference by a lack of data in patient files. Also, the countries of sub-Saharan Africa, unlike the countries of the Maghreb, are countries with a high prevalence of tuberculosis, tuberculosis infection can therefore go unnoticed.

Sixty-two patients, or 47% of the patients in our study, had received BCG vaccination; the status

of the other patients with regard to this vaccination was unknown. Loubna in his series found 71.6% of patients vaccinated against tuberculosis with BCG. Since BCG vaccination coverage in 2013 was estimated at 95.3% in Togo [11], the low percentage of BCG vaccination in our study can be explained by an underestimation of this vaccination. BCG vaccination would reduce the occurrence of extrapulmonary tuberculosis, particularly in children [12]. In our study, 33.3% of patients had at least one comorbidity. HIV infection was found in 21.2% of patients. Some studies indicated a large proportion of HIV-infected patients among patients with extrapulmonary tuberculosis, notably that of Yone et al. in Cameroon which found a proportion of 47.7% [13]. Razik et al. in his series of 287 cases of extrapulmonary tuberculosis at the university hospital of Oran in Algeria, found 56% cases of HIV infection [14]. The immunosuppression induced by this infection favors the occurrence of extrapulmonary tuberculosis. In our study, 4.6% of patients had diabetes. Loubna in his study at Morocco found diabetes in 7% of patients [10]. Nuiakh, in his study in Morocco on 156 cases of cervical lymph node tuberculosis, found diabetes in 27.56% of patients [15]. Diabetes, especially when it is poorly controlled, increases the risk of tuberculosis, whether pulmonary or extrapulmonary.

We found alcohol consumption in 18.2% of patients and smoking in 9.1% of patients. Loubna in his study in Morocco found smoking in 47.2% of patients, alcohol consumption in 2% of patients and cannabis consumption in 11.2% of patients [10]. These results support the presence of comorbidities and drug consumption in patients with extrapulmonary tuberculosis. These factors induce immunosuppression favoring the occurrence of extrapulmonary tuberculosis.

LOCATION OF TUBERCULOSIS

In our study we found a predominance of osteoarticular involvement (53.0%) followed by pleural involvement (21.2%). In the literature, several authors describe a predominance of lymph node and pleural involvement. This is the case of Gater et al. in Algeria, who in their cohort of 151 patients reported a predominance of lymph node involvement at 47.7% followed by pleural involvement at 29.8% [16]. This is also the case of Ajmi et al. [17], who in their series found a predominance of lymph node involvement at 52% followed by pleural involvement at 16%. This is also the case for Antoine et al. in France [18], and TeBeek et al. in Holland who reported a lymph node predominance with a proportion of 54.8% and 39% respectively [19].

The predominance of osteoarticular localization in our study can be explained by the fact that tuberculous spondylodiscitis constitutes the main differential diagnosis of spondylodiscitis caused by common organisms, thus motivating the diagnostic presumption of tuberculosis in the absence of favorable evolution under antibiotic therapy. well-managed non-specific

spondylodiscitis previously considered to have a common cause.

DIAGNOSTIC MEANS

In our study, 28 patients (21.2%) had a definitive diagnosis. The definitive diagnosis was histological in 12.1% of cases. Some studies show a higher percentage of diagnostic certainty, notably that of Loubna in Morocco [10] and Hentati et al. in Tunisia [20] (Table XIV).

Table XIV: Diagnostic method based on studies

	Our study	Loubna(Morocco)	Hentati et al. (Tunisia)
Histology	12,1 %	76%	48%
Molecular (GeneXpert)	7,6 %	2 %	0 %
Bacteriology	1,5 %	8 %	12 %
Presumption	78,8 %	14 %	40 %

In developed countries, there is a higher rate of diagnostic certainty. This is the case of the study conducted by the Center for Disease Control and Prevention in the United States of America which in its 2009 publication reported 71% positive cultures in cases of extrapulmonary tuberculosis [21]. The high diagnostic confirmation rate in developed countries can be explained by the advanced technical platform and laboratory performance.

In our regions, we are witnessing on the one hand the insufficiency of the technical platform, and on the other hand an insufficient financial means for the diagnostic management of a disease which mainly affects young people of low socio-economic level.

Histological study remains the most widespread means of confirmation because the sensitivity of bacteriology is low, and molecular biology is not sufficiently available in our regions. Certain forms of tuberculosis are more accessible to biopsy, notably lymph node and pleural involvement, explaining the greater frequency of diagnostic confirmation in these cases.

The diagnostic presumption is still common practice in our regions, especially for forms that are difficult to access by biopsy, in particular osteoarticular damage, explaining the proportion of high diagnostic presumption in these cases.

THERAPEUTIC AND EVOLUTIONAL ASPECTS

All patients in our study received the 4 first-line anti-tuberculosis drugs (RHZE) during the initial intensive phase because no resistance to Rifampicin was documented. This is the case of the patients in the Loubna study in Morocco, Derrar et al. in Algeria and Hamrouni et al. in Tunisia [9, 10, 22]. In fact, the therapeutic regime proposed by the WHO and adopted by several countries for the treatment of tuberculosis with susceptible bacilli is the same for pulmonary and

extrapulmonary tuberculosis. Only the duration can be extended for osteoarticular and neurological tuberculosis.

In our study, adjuvant corticosteroid therapy was prescribed in all cases of pericardial tuberculosis. This corticosteroid therapy was also prescribed in all cases of multifocal tuberculosis, because these multifocal conditions all included pericardial involvement. In certain cases of osteoarticular tuberculosis such as cases of spondylodiscitis with disabling lower back pain, corticosteroid therapy was for decompressive purposes.

In our study, the hospital outcome was favorable in 97.0% of cases. Hamrouni et al. in Tunisia found an initial favorable development in 73% of cases [9]. This demonstrates the benefit of making the diagnosis of extrapulmonary tuberculosis earlier in order to initiate appropriate treatment.

CONCLUSION

Our study allowed us to identify 132 cases of extrapulmonary tuberculosis during the study period. We found that all age groups were affected with a predominance of young subjects aged 20 to 60 years. The most common comorbidity was HIV infection. HIV infection was significantly associated with intrahospital outcome.

The diagnosis of extrapulmonary tuberculosis was mainly presumptive, in relation to the limited technical platform, the average performance of our laboratories, and the insufficient financial resources of patients. The confirmatory diagnosis was mainly histological. Osteoarticular involvement was the most common location in our study (53% of patients) followed by pleural involvement.

Standard therapeutic management of tuberculosis was instituted according to the recommendations of the National Tuberculosis Control Program, giving good results with an overall favorable initial evolution.

Our sample, although limited, allowed us to have an overview of this pathology at the Sylvanus Olympio university hospital center in Lomé. A study on a larger sample size could provide more precise results.

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CONFLICTS INTERETS : No conflicts

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