



## Original article

## Frequency and risk factors for Miliaria Tuberculosa in Bangui

Fréquence et facteurs de risques de la miliaire tuberculeuse à Bangui

G Tekpa<sup>1,2</sup>, P Wili-koé\*<sup>1</sup>, J Koma Zobanga<sup>3</sup>, G Ngai Eudes<sup>2,4</sup>, F Padou<sup>1</sup>, T Mobima<sup>2,5</sup>**Abstract**

**Introduction:** We conducted this study to describe the epidemiological and clinical profiles of patients with tuberculosis miliaria and to identify risk factors for the disease.

**Methodsology:** This was a case-control study of patients with tuberculosis miliaria (cases) and non-tuberculosis (controls), who were followed between 1 April 2010 and 31 December 2017 at the Friendship Hospital in Bangui.

**Results:** A total of 192 patients were included, including 96 cases of miliaria tuberculosa and 96 controls. The mean age was 40.9±14.1 years [20; 87] for cases compared to 36.6±4.4 years [20; 45] for controls. The sex ratio was 1.2 in cases compared to 1 in controls. The in-hospital frequency of miliaria tuberculosis was 15.5% out of a total of 621 tuberculosis cases. The frequency of TB/HIV co-infection was 69.7% (108/155). The median CD4 T cell count was 100/mm<sup>3</sup> [1; 646] in cases versus 100/mm<sup>2</sup> [1; 1079] in controls. The case fatality rate was

35.4% compared to 33.3% for controls. HIV infection was the risk factor for miliaria tuberculosis ( $p = 0.04$ ; OR=2.1[1.1-4.5]). Ko

**Conclusion:** In the Central African Republic, the hospital incidence of tuberculosis miliaria in Bangui is high, and HIV is associated with its occurrence. Effective preventive measures could reduce the incidence of this disease.

**Keywords:** Miliaria tuberculosis, epidemiology, Bangui.

**Résumé**

**Introduction :** Nous avons mené, cette étude pour décrire les profils épidémiologique et clinique des patients atteints de la miliaire tuberculeuse et identifier les facteurs de risque de la maladie.

**Méthodes :** Il s'agissait d'une étude cas-témoins portant sur les patients atteints de miliaire tuberculeuse (cas) ou non (témoins), qui ont été suivis entre le 1er avril 2010 et le 31 décembre 2017 à l'hôpital de l'amitié de Bangui.

Résultats : Au total de 192 patients ont été inclus, dont 96 cas de miliaire tuberculeuse et 96 témoins. L'âge moyen était de 40,9±14,1 ans [20 ; 87] pour les cas contre 36,6±4,4 ans [20 ; 45] chez les témoins. Le sex-ratio était de 1,2 chez les cas contre 1 chez les témoins. La fréquence hospitalière de la tuberculose miliaire était de 15,5 % sur un total de 621 cas de tuberculose. La fréquence de la co-infection tuberculose/VIH était de 69,7 % (108/155). Le nombre médian de lymphocytes T CD4 était de 100/mm<sup>3</sup> [1 ; 646] chez les cas contre 100/mm<sup>2</sup> [1 ; 1079] chez les témoins. Le taux de létalité était de 35,4 % contre 33,3 % pour les témoins. L'infection par le VIH était le facteur de risque de tuberculose miliaire (p = 0,04 ; OR=2,1[1,1-4,5]). Ko

Conclusion : En République centrafricaine, l'incidence hospitalière de la miliaire tuberculeuse à Bangui est élevée, et le VIH est associé à sa survenue. Des mesures préventives efficaces pourraient réduire l'incidence de cette maladie.

Mots-clés : Tuberculose miliaire, épidémiologie, Bangui.

## Introduction

Miliaria tuberculosa is a serious form of tuberculosis that is life-threatening. It is due to the lymphohaematogenous dissemination of tuberculous bacilli from a ruptured focal lesion in the blood or lymphatic flow at one or more points in the body (1), (2), (3), (4). Before the era of antibiotics, it was common in children under three years of age, in whom its incidence had declined thanks to the tuberculosis vaccine. Currently, a spike is observed in adolescents and young adults, probably due to the HIV epidemic and the decline in iatrogenic or natural cellular immunity (4),(5), (6) .

Tuberculosis miliaria accounts for less than 2% of tuberculosis according to some authors and about 8% of extrapulmonary tuberculosis in immunocompetent patients (4). While the formal diagnosis of tuberculosis is based on the presence of the bacilli

on direct examination, tissue culture or secretions, the diagnosis of miliaria is most often radioclinical, due to the rarity of positive bacilloscopies and the urgency of treatment. Increasingly common among people living with HIV (PLHIV)(7), (8), (9) , miliaria requires special attention.

In Africa, the frequency of tuberculosis miliaria varies according to the authors. In 2000, it was estimated at 5.1% in Burkina Faso, with a case fatality rate of 44.44%(9) . In Morocco in 2017, the frequency of miliaria was estimated at 0.56% of all admission cases during the study period, with a miliary tuberculosis-HIV co-infection at 4.9% and a mortality rate of 13.5%(10). In Central Africa, a study carried out in Cameroon in 2017 reported a prevalence of 16.1%, with HIV infection (58.4%), alcoholism (38.9%) and smoking (20.8%) as the main contributing factors(11) .

In the Central African Republic (CAR), a study on the prevalence of tuberculosis-HIV co-infection in hospitals in Bangui in 2014 reported a frequency of 3.1% of tuberculosis miliaria (12). This work was carried out on the assumption that there are multiple risk factors for tuberculosis miliaria in Bangui. The objective of our work was to describe the frequency of tuberculosis miliaria and to identify risk factors for its occurrence in order to improve disease control strategies.

## Methodology

### • Site and type of study

The study was carried out in the infectious diseases and hepato-gastroenterology departments of the Friendship University Hospital in Bangui.

This was a case-control study of TB cases recorded between 1 April 2010 and 31 December 2017.

### • Study population

It was made up of all patients admitted to hospitalization for tuberculosis during the study period.

### • Inclusion criteria and data collection

### • Case Inclusion

We included in our study consecutively, all patients

in whom a diagnosis of tuberculosis miliaria was made on clinical and radiological grounds and who received anti-tuberculosis treatment in accordance with the guidelines of the national tuberculosis control program.

- Inclusion of Witnesses

The controls were patients with pulmonary tuberculosis without miliary images and without extrapulmonary locations, who had the same socio-economic profile and who were admitted to the same departments during the study period. A witness was retained for a case of miliary tuberculosis.

In order to confirm or rule out the diagnosis of tuberculosis miliaria, all chest x-rays of the cases and controls were interpreted by a radiologist.

- Data collection

Data were collected retrospectively using an anonymous questionnaire. For each case of miliary tuberculosis included, we collected sociodemographic, clinical and radiological data. The dependent variable was the occurrence of tuberculosis miliaria, and the independent variables were the sociodemographic characteristics of the patients (age (sex, level of education, occupation), clinical (history/field) and paraclinical parameters. For each control, we recorded sociodemographic and clinical characteristics.

- Data Entry and Analysis

The implementation of the study has received prior authorization from the Ethics and Scientific Committee of the Faculty of Health Sciences of the University of Bangui. The data was entered using Microsoft Office Excel and analysed using the Epi info 7 software. The processing of the data has been done in strict confidentiality. Qualitative variables were summarized as a proportion and quantitative variables as a mean or median. For the comparison of proportions, we used the chi-square test. A difference between two proportions was significant when  $p < 0.05$ .

## Results

- General characteristics of the study population and frequency of the Tuberculosis Miliaria

We included a total of 192 TB patients, divided into 96 cases and 96 controls. There were 101 males (52.0%), resulting in a sex ratio of 1.1. This sex ratio was 1.2 for cases and 1 for controls. The mean age was  $40.9 \pm 14.1$  years (median = 45 years [20; 87]) in cases and  $36.6 \pm 4.4$  years (median = 37 years [20; 45]) in controls. The 25-44 age group accounted for 68.2% of the total, with 69.9% of cases and 66.8% of controls (Table I). Bangui was the place of residence of 82.3% of the cases compared to 72.9% of the controls. Unemployed patients, civil servants, housewives and students were represented in 19.8 per cent and 17.7 per cent, 9.4 per cent and 7.9 per cent of the cases, respectively, compared with 3.1 per cent, 17.7 per cent, 39.6 per cent and 5.2 per cent of controls. Out of a total of 16 smoking patients (15.6%) with miliary tuberculosis, there were 15 males (93.7%) and one female (6.2%), with a significant difference ( $p = 0.0002$ ). The proportion of patients vaccinated against tuberculosis was the same in cases and controls (96.8%). There were 15 cirrhotic patients with miliary tuberculosis, or 15.6%, males accounted for 66.7% (10 cases) and females 33.3% (5 cases), with no significant difference ( $p = 0.175$ ). A total of 108 out of 155 TB/HIV co-infected patients (69.7%) had TBD4 cell counts. The median TCD4 lymphocyte count was 100/mm<sup>3</sup> [1 - 646] in cases versus 100/mm<sup>3</sup> [1-1079] in controls. The time to consultation (the period between the onset of symptoms and the date of consultation) ranged from 1 to 87 days in cases compared to 6 to 130 days in controls. The length of hospital stay was  $14.6 \pm 12$  days for cases versus  $18.4 \pm 13.5$  days for controls.

The outcome of patients at the end of treatment was marked by a proportion of 15.6% (n=15 cases) of lost to follow-up in cases compared to 5.2% (n=5 cases) in controls, and the case fatality rate was estimated at 35.4% (94.1% of patients who died were HIV-infected) in cases compared to 33.3% in controls

(40% were HIV-infected).

During the study period, 96 cases of tuberculosis were recorded out of the 621 cases of tuberculosis in all forms, i.e. a hospital frequency of 15.5%. This frequency varied throughout the study period [Figure 1].

• Risk factors for miliary tuberculosis

There was no statistically significant association

between the occurrence of tuberculosis miliary and sociodemographic characteristics. The frequency of tuberculosis miliary was higher in cirrhotic patients, but without significant difference compared to those without cirrhosis. On the other hand, we observed a statistically significant association between HIV infection and the occurrence of tuberculosis miliary [Table II].

Table I: Age group of study participants recruited in hospitalization in the infectious and tropical diseases and hepato-gastroenterology departments of the Bangui Friendship University Hospital from April 1, 2010 to December 31, 2017.

Age range (years)	Case (number; %)	Controls (number; %)	Total (%)
≤24	4(4,2)	4(4,2)	8(4,2)
25-34	33(34,4)	35(36,4)	68(35,4)
35-44	34(35,4)	29(30,2)	63(32,8)
45-54	14(14,6)	23(24,0)	37(19,3)
≥55	11(11,4)	5(5,2)	16(8,3)
Total	96(100,0)	96(100,0)	192(100,0)



Figure 1: Hospital frequency of tuberculosis miliary among patients admitted to hospitalization between 2010-2017 in the infectious diseases and hepato-gastroenterology departments of the CHU de l’Amitié in Bangui (N=96).

Table II: Relationship between sociodemographic characteristics, terrain and the occurrence of tuberculosis miliaria in study participants, recruited in hospitalization in the infectious and tropical diseases and hepatogastroenterology departments of the Central African Sino Friendship University Hospital in Bangui from April 1, 2010 to December 31, 2017.

Parameters	Case (n, %)	Controls (n, %)	GOLD [95% CI]	p
<b>Socio-demographic characteristics</b>				
<b>Sex</b>				
Male (n=101)	53(52,5)	48(47,5)	1,2[0,7-2,2]	0,47
Female (n=91)	43(47,2)	48(52,8)	1	
<b>Age</b>				
< 55 (n=176)	85(48,3)	91(51,7)	0,4[0,14-1,27]	0,12
≥ 55(n=16)	11(68,7)	5(31,3)	1	
<b>Terrain</b>				
<b>Cirrhosis</b>				
Yes (n=22)	15(68,2)	7(31,8)	2,2[0,9-6,1]	0,69
No (n=170)	81(47,6)	89(52,4)	1	
<b>HIV status</b>				
HIV+ (n=155)	83(53,5)	72(46,5)	2,1[1,1-4,5]	0,04
HIV- (n=37)	13(35,1)	24(64,8)	1	
<b>Tobacco</b>				
Yes (n=31)	16(51,6)	15(48,4)	1,1[0,5-2,3]	0,84
No (161)	80(49,7)	81(50,3)	1	

## Discussion

Data on the frequency of tuberculosis miliaria are scarce in the Central African context. Miliary tuberculosis cases are often not specified in the progress reports of the national tuberculosis control programme. Using data from the CHU de l'Amitié in Bangui, we were able to assess the frequency of the disease and identify the factors associated with its occurrence.

Our results show that tuberculosis miliaria remains a very common pathology in Bangui. Males were more affected by Tuberculous Miliaria than females. This male predominance has been observed in several studies conducted in Africa, but it has not been consistent. In Burkina Faso in 2000, Senegal in 2017 and Mali in 2018, male predominance was described with sex ratios of 2.4, 2.4 and 1.3 respectively (9), (13),(14) . In 2017, authors from Morocco and Cameroon described a female predominance during their work on the tuberculosis miliaria (10), (11).

This sex ratio in favour of men in our study could be related to the high frequency of risk factors for tuberculosis miliaria (smoking and cirrhosis) in this group. Our sample was mainly composed of young adults, with the age group of 25-44 years being the most represented. The high incidence of TB miliaria in this age group may be explained by the high incidence of HIV infection, which was 68.8% among cases in this age group. Depending on the socio-professional conditions of the patients, the tuberculosis miliaria was observed in all social strata. This trend may be related to the polymorphism of the risk factors for the disease. According to the literature, BCG vaccination protects against severe forms of tuberculosis, such as meningeal disease and tuberculosis miliaria in children (15). Our results would be in line with the hypothesis put forward by Bitchong et al in Cameroon that BCG protection is not very effective in adults(16) . The median CD4 T cell count was low in patients living with HIV. This value would explain the severity of immunosuppression caused by HIV, which could



promote the development of military tuberculosis. The consultation time for military tuberculosis cases was shorter than for controls.

This could be related to the acute manifestation seen in Empis' typhoid (acute manifestation of tuberculosis miliaria) as opposed to a slow manifestation which is much more observed in common pulmonary tuberculosis. The average length of stay of TB cases ( $14.61 \pm 12$  days) was lower than in Mali in 2017, which was 65 days (14). This short length of stay in our study could be explained by the early onset of death.

This study allowed us to determine the hospital frequency of this disease for the period from April 2010 to December 31, 2017. Tuberculosis miliaria has been a major cause of morbidity, with a steady increase in the frequency of hospitalizations after the military-political crisis of 2013 with a frequency of 5.2%. However, it was difficult to compare our results with those of other studies conducted in different settings, often in specialized and better-equipped centers. This situation is largely linked to the socio-political unrest in the capital Bangui in 2013, which led to a drop in hospital attendance during this period. However, the hospital frequency of Miliaria TB in our study was higher than that reported by several authors in Africa (8),(17). This could be linked to the high prevalence of HIV, the main risk factor for tuberculosis in our context. The proportion of cases lost to follow-up among the cases in our study was higher than that reported in controls. This observation could be in agreement with that of Bitchong et al in Cameroon in 2021, who showed that patients have good adherence to their treatment when the etiology is identified (16). According to the literature, Miliaria Tuberculosa is usually fatal if left untreated. The prognosis remains guarded even with adequate treatment, with a mortality rate of 25 to 30% in adults and 15 to 20% in children (18).

Several independent prognostic factors have been identified, including advanced age, central nervous system involvement, hypoalbuminemia, renal failure, late diagnosis and late initiation of anti-tuberculosis

therapy (19). The case fatality rate in our study was lower than those reported by the authors from Burkina Faso (9). In contrast, our case fatality rate was higher than those reported in Morocco in 2017 and Cameroon in 2021(10), (16). This difference could be explained by the variation in disease endemicity from region to region and the disparity of the selection criteria used in the different series.

#### • Risk factors for Miliaria Tuberculosis

The factor associated with the occurrence of tuberculosis miliaria was HIV infection. HIV-induced immunosuppression is thought to be the cause of the hematogenous dissemination of *M. tuberculosis* from the pulmonary focus. This risk factor was found in a study conducted in Cameroon in 2017(11). According to the literature, many authors report alcohol and tobacco use as the main risk factors for military tuberculosis(20). These factors were not significantly associated with the occurrence of miliaria tuberculosa in our work, probably due to the small size of our sample.

#### **Conclusion**

Miliaria is a severe form of tuberculosis in Bangui. It is promoted by HIV infection. Our results suggest that better control of HIV infection and the implementation of isoniazid chemoprophylaxis may reduce the importance of this form of TB.

#### **Prior Knowledge**

- Rare pathology and very common in immunocompromised people;
- Radio-clinical diagnosis with a rarity of bacilli on direct examination;
- High case fatality rate despite TB treatment.

#### **Current knowledge**

- High hospital frequency;
- All social strata concerned;
- HIV infection is the main cause.

### Authors' contributions

All authors contributed to the conduct of the research. All authors have read and approved the final version of the manuscript.

### Thanks

We would like to thank the academic authorities of the Faculty of Health Sciences for allowing this study to be conducted, and the staff of the Department of Infectious and Tropical Diseases for their support in the organization of the study.

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### \*Correspondence :

Wili-koé Prince

[princewilikoe@yahoo.fr](mailto:princewilikoe@yahoo.fr)

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- 1 : Infectious Diseases Department, Friendship University Hospital, Bangui, Central African Republic;
- 2 : Faculty of Health Sciences, University of Bangui, Central African Republic;
- 3 : World Health Organization, Bangui, Central African Republic;
- 4 : Armed Forces Health Service, Bangui, Central African Republic;
- 5 : Department of Radiology and Imaging, University of Bangui, Bangui, Central African Republic;

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**Conflict of interest :** None

### References

- [1] Barker RD. Clinical tuberculosis. *Medicine*. 2008;36(6):300-5.
- [2] Carette MF, Azeucot N, Le Blanche A, Le Breton C, Bigot JM. Apport de l'imagerie dans le

diagnostic et le suivi de la tuberculose thoracique. *Rev Pneumol Clin*. 1994;50:229-39.

- [3] Escobedo-Jaimes L, Cicero-Sabido R, Criales-Cortez J, Ramirez E, Romero M, Rivero V, et al. Evaluation of the polymerase chain reaction in the diagnosis of miliary tuberculosis in bone marrow smear. *Int J Tuberc Lung Dis*. 2003;7(6):580-6.
- [4] Kwong JS, Carignan S, Kang EY, Muller NL, FitzGerald JM. Miliary tuberculosis: diagnostic accuracy of chest radiography. *Chest*. 1996;110(2):339-42.
- [5] Chastonay P. Late disseminated tuberculosis. Anatomico-clinical correlations in 40 cases. *Rev Mal Respir*. 1989;6(5):425-8.
- [6] Bissagnene E, Die-Kacou H, Eba F, Coulibaly G. Guide diagnostique et thérapeutique de l'infection à VIH en Afrique. Edition GUT; 1999.
- [7] Huchon G. Infection tuberculeuse et tuberculose pulmonaire de l'adulte. *Rev Mal Respir Suppl*. 1997;14(5):5S49-59.
- [8] N'Dhatz M, Domoua K, Coulibaly G, Traore F, Kanga K, Konan JB, et al. Aspects of thoracic radiography of patients with tuberculosis and HIV infection in Ivory Coast. *Rev Pneumol Clin*. 1994;50(6):317-22.
- [9] Ouédraogo M, Ouédraogo G, Ouédraogo SM, Zoubga ZA, Bambara M, Ky C, et al. Aspects épidémiologiques et cliniques des miliaires tuberculeuses au Burkina Faso: A propos de 93 cas. *Med Afr Noire*. 2000;47:420-2.
- [10] Zaghba N, El Hachimi K, Benjelloun H, Yassine N. La miliaire tuberculeuse, une série rétrospective marocaine. *Rev Pneumol Clin*. 2018;74(1):28-34.
- [11] Ahibena LE, Bitchong CE, Massongo M, Sine VR, Ze EA. Aspects épidémiologiques, cliniques, paracliniques et évolutifs de la miliaire tuberculeuse à l'hôpital Jamot-de-Yaoundé. *Rev Mal Respir*. 2018;35
- [12] Prevalence de la co-infection tuberculose et

VIH à Bangui. [Internet]. Disponible sur: <https://www.researchgate.net/scientific-contributions/kosh-komba-J-20064612576>

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<https://doi.org/10.70065/24JINF63.001L042708>

[13] Miliare tuberculeuse au service de pneumologie du CHU de Fann en 2017, Dakar: A propos de 51 cas. [Internet]. Disponible sur: <https://www.researchgate.net/publication/312204400>

[14] Tuberculose miliare: Profil épidémio-clinique en 2018. [Internet]. Disponible sur: <https://www.sciencedirect.com/science/article/abs/pii/S0761842517309142>

[15] Fréquence et évolution de la co-infection VIH-tuberculose chez l'adulte à l'hôpital presbytérien de Mbuji-Mayi. [Internet]. [cité 24 mai 2024]. Disponible sur: <https://www.memoireonline.com/08/15/9247/>

[16] Ekono CB, Ze JJ, Azoumbou MT, Massongo M, Awana AP, Komo EN, et al. Miliare tuberculeuse bacillifère: Aspects épidémiologiques, cliniques et paracliniques à l'Hôpital Jamot de Yaoundé. [Internet]. [cité 24 mai 2024]. Disponible sur: <https://www.researchgate.net/publication/353286160>

[17] Patterson JE. A Clinician's Guide to Tuberculosis. Michael D. Iseman; Philadelphia, PA: Lippincott Williams & Wilkins; 2000. 448 p. *Infect Control Hosp Epidemiol.* 2001;22(5):322-3.

[18] Sharma SK, Mohan A, Sharma A, Mitra DK. Miliary tuberculosis: new insights into an old disease. *Lancet Infect Dis.* 2005;5(7):415-30.

[19] Dischl B, Bellini C, Rochat S, Büla C. Tuberculose miliare chez une personne âgée: diagnostic inattendu à l'autopsie. *Rev Med Suisse.* 2010;(270):2135.

[20] Fouzi S, Ketata FW, Marwen I, Msaad S, Yangui AA. La miliare tuberculeuse: à propos de 29 cas. *Rev Tunis Infectiol.* 2010;46-52.