Research Article ISSN 2639-9458

Microbiology & Infectious Diseases

# Neuromeningeal Tuberculosis at The Brazzaville University Hospital: Prevalence and Associated Factors

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**Received:** 22 December 2019; **Accepted:** 19 February 2020

**Citation:** Ossibi Ibara BR, Ekat M, Atipo-Tsiba PW, et al. Neuromeningeal Tuberculosis at The Brazzaville University Hospital: Prevalence and Associated Factors. Microbiol Infect Dis. 2020; 4(1): 1-5.

## ABSTRACT

***Goal:*** *To determine the prevalence of neuromeningeal tuberculosis in Brazzaville University Hospital and to investigate the associated factors.*

***Patients and Method:*** *Data was collected from cases of neuromeningeal tuberculosis admitted to the Infectious Diseases Service of the University Hospital of Brazzaville during the period from March 1, 2014 to March 31, 2019.*

***Results:*** *Fifty-six patients included (1.38% of admissions) with an average age of 42 ± 11.7 years (range, 23 to 70 years), mostly female (n = 38, 67.9%) with a sex- ratio of 0.5; unemployed (n = 20, 35.71%), urban residents (n = 51, 91.1%) and single (n = 29, 51.8%). 17 patients (30.4%) had a history of tuberculosis; 83.9% of the patients were HIV positive. The main reasons for consultation were Fever (n = 56, 100%), behavioral disorders (n = 25, 44.6%), and consciousness disorders (n = 22, 39.3%). The average consultation time was 15 days (range: 1 and 26 days). AEG (n = 51, 91.1%), the main signs of examination were impaired consciousness (n = 96, 4%), and stiff neck (n = 17, 30.35%). Five patients (8.9%) were found with ophthalmological abnormalities including tubers of Bouchut. The appearance of the LCS was clear (73.2%), disorder (1.8%), hyperproteinorrheia (68.9%), hypoglycorachia (91.1%). A localization associated with TNM was found in 34 cases (60.7%) dominated by pulmonary involvement in 21 cases (61.8%). The treatment duration was 5 days on average (range 0 to 18 days). Overall lethality was 53.6%, mainly due to severe anemia (n = 10, 33.3%).*

*Age (SHR = 3.5, CI: 1.14-9.29, P = 0.03), Treatment (SHR = 0.67, CI: 0.57-0.79, P = 0, 00) and route of administration (HR: 3.71, CI: 1.62-8.48, P = 0.002) influenced the death of patients with a probability of survival in untreated patients between 6-7 days = 0.28, IC; 0.01-1.61 and in patients treated between 6-7 days = 0.93; IC: 0.82-0.97.*

## Keywords

Tuberculosis, Neuromeningeal, Prevalence, Associated factors, CHU, Brazzaville.

## Introduction

Tuberculosis is a major public health problem leading to high morbidity and mortality, especially in the population immunocompromised by HIV [1]. It is a transmissible infectious disease caused by a mycobacterium belonging to the tuberculosis complex called Koch's bacillus (BK). Its main localization is the lungs, but other organs such as the brain can be affected, giving rise to extra-pulmonary localizations [1,2].

The neuro-meningeal localization or neuro-meningeal tuberculosis (TNM) is one of the most severe expressions of this disease with a mortality of between 5% and 44% despite the precocity and the

quality of the management of this condition [3-5]. Its diagnosis is often difficult through clinical polymorphism and the weakness of the technical plateau observed in our regions. In Congo, the prevalence of tuberculosis in all localities is 12% [ 6]; that of pulmonary tuberculosis in the Service of Infectious Diseases is 10.5% [7], whereas the part of the neuromeningeal localization of tuberculosis has not yet been established at the CHU of Brazzaville, hence the relevance of the present study whose general objective is to determine the hospital prevalence of the neuro-meningeal tuberculosis and identify the associated factors. More specifically, the study aimed to describe the epidemiological, clinical and diagnostic features of patients with TNM, describe the evolutionary aspects of these patients before identifying the likelihood of their survival in the care setting.

## Patients and Methods

The study covers patients at least 17 years of age, regardless of their immunologic status with HIV, whether or not they received triple antiretroviral therapy or were hospitalized during the study period for TNM. It was a cross-sectional, descriptive and analytical study conducted in the Infectious Diseases Service at the Brazzaville University Hospital for a period of 60 months between March 1, 2014 and March 31, 2019.

The diagnosis of TNM was made on the basis of a bundle of epidemiological, clinical, biological, morphological and also therapeutic arguments in accordance with the diagnostic schemes established by the British infection Society [81] while taking into account the weakness of the hospital technical platform.

Study variables were socio-demographic (age, sex, occupation, place of residence, level of education, marital status, socio-economic level, narrow tuberculosis relationship, history of tuberculosis) clinical (pattern admission, consultation time, neurological examination, fundus examination), paraclinical (brain scanner, cerebrospinal fluid study, blood cultures, HIV status, viral load and CD4 count, frontal chest x-ray), therapeutic (time to management, modalities of administration of TB treatment) and progressive (length of stay, probability of survival, number and causes of death).

Operational Definitions [8]
Low socio-economic level
The socio-economic level was low according to one of the following items:
Patient living in community, institution or homeless;
Patient with no access to drinking water or electricity;
Monthly income less than 200,000 FCFA.

### New cases of tuberculosis

These are patients who have never received antituberculosis treatment or have been treated for less than one month.

### Patients with relapsed tuberculosis

These are patients who have already received anti-tuberculosis treatment, who were at the end of their last course of treatment, classified as a cure or completed treatment, and are now diagnosed with a recurrent episode of tuberculosis.

### Patients treated after being lost to follow-up

These are patients who have already received anti-tuberculosis treatment and have been reported lost to follow-up.

### Statistical analyzes

The data was collected on Excel® and then transferred to Stata 12 (College Station, Texas 77845 USA) for analysis. Quantitative variables were presented in terms of numbers and percentage, qualitative variables on average ± standard deviation and their extremes. The results of the competitive risk model were presented in Hazard Ratio (SHR) with a 95% confidence interval (95% CI). The Kaplan-Meier curve was used to calculate the overall probability of death during hospitalization for neuro-meningeal tuberculosis, and to compare the probabilities of death by taking into account whether or not TB treatment was used, the Log test -Rank has been used. Factors associated with deaths during hospitalization for neuro-meningeal TB were identified with the competitive risk model. Variables with a $p < 0.20$ value in univariate analysis were used for multivariate analysis. For all statistical analyzes, the threshold of significance was set at $p < 0.05$.

## Results

A total of 56 cases of neuro-meningeal tuberculosis (1.38% of admissions) with average age 42 ± 11.7 (23-70) years, predominantly female (n = 38, 67.9%) with sex ratio F / H = 2.1. Patients were unemployed (n = 20, 35.7%), public servants (n = 15, 26.8%), single (n = 29, 51.8%), common-law unions (n = 9, 16.1%) %) at the primary education level (n = 32, 58.2%) and with a low socio-economic level (n = 36, 64.3%). 17 patients (30.4%) had a history of tuberculosis including 14 cases of pulmonary localization and 51.8% of patients did not know their serologic status with respect to HIV on admission. The mean time to view was 15 ± 2.5 (3-31) days for consciousness disorders and fever (n = 25, 44.6%), febrile seizures (n = 16, 28.6%) and headache febrile (n = 58%). The examination found an AEG (n = 51, 91.1%), mucous pallor (n = 35, 62.5%), obstruction (n = 23, 41.1%), left hemiplegia (n = 35; = 3, 5.4%), meningeal stiffness (n = 17, 30.4%). Ophthalmologically, in five patients (8.9%), the examination showed on both sides a visual decline with visual acuity far to 3/10 non-improvable, moderate hyalitis, a large retinal vasculitis with tubers Bouchut scattered at the posterior pole.

CSF was clear (n = 41, 73.2%) with mean cytorachia of 58 ± 1.3 (1-940) cells / mm3, mean protein ratio of 1.35 ± 1.0 (0.2-15). 2) g / l and mean glycoprecia of 0.33 ± 0.1 (0.1-0.9) g / l. the mean Hb value was 8.7 ± 0.9 (6-15.3g / dl). The brain scan was performed in only 13 cases and was normal (n = 7, 53.9%), it showed a hypodense lesion without contrast enhancement (n = 2, 15.4%). HIV serology was positive (n = 47, 83.9%). The associated sites were pulmonary (n = 21, 37.5%), lymph node (n = 3, 5.4%), the mean time to start anti-tuberculosis treatment was 5 ± 0.3 (0-18 days). These were new cases (n = 34, 69.4%) and treatment was given orally (n = 35, 71.4%). The mean duration of hospitalization

was 14 ± 1.2 (1-60) days and lethality was found in 30 patients (53.6%). The mean time to death was 6 ± 0.2 (0-60) days for anemia (n = 10, 33.3%) (Table 1). Age (SHR = 3.5, CI: 1.14-9.29, P = 0.03), Treatment (SHR = 0.67, CI: 0.57-0.79, P = 0, 00) and route of administration (HR: 3.71, CI: 1.62-8.48, P = 0.002) had an influence on patient death (Table 2) with a probability of survival in untreated patients between 6-7 days = 0.28, IC; 0.01-1.61 and in patients treated between 6-7 days = 0.93; IC: 0.82-0, 97 (Figures 1 and 2).

| Death Causes | n | % |
|---|---|---|
| Severe anaemia | 10 | 33,3 |
| Septic shock | 7 | 23,3 |
| Respiratory distress | 7 | 23,3 |
| Hydroelectrolytic disorders (hyperkalaemia) | 2 | 6,8 |
| Unspecified | 4 | 13,3 |

**Table 1:** Causes of patient death.

| Variables | Association | SHR | IC à 95% | P<0,05 |
|---|---|---|---|---|
| Age | < 42 years | Reference | | |
| | ≥42 years | 3,21 | 1,12-9,16 | 0,03 |
| Consultation ≥15 days | Yes | Reference | | |
| | No | 2,11 | 0,77-5,78 | 0,15 |
| HTIC Signs | No | Reference | | |
| | Yes | 2,72 | 0,96-7,72 | 0,06 |
| Glasgow | 13-15 | Reference | | |
| | 8-12 | 1,73 | 0,62-3,33 | 0,40 |
| | 6-7 | 1,56 | 0,11-16,64 | 0,81 |
| Treatment | No | Reference | | |
| | Yes | 0,67 | 0,58-0,78 | 0,00 |
| Administration route | Oral | Reference | | |
| | SNG | 3,71 | 1,62-8,48 | 0,002 |

**Table 2:** Death associated factors.

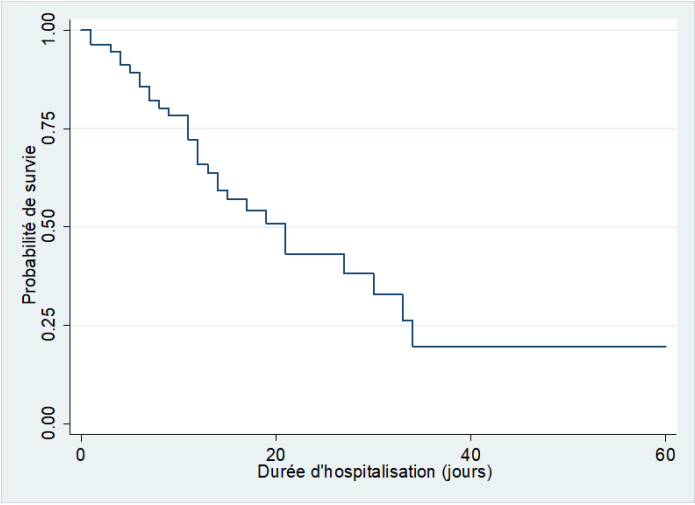


**Figure 1:** Probability of overall survival of hospitalized patients.

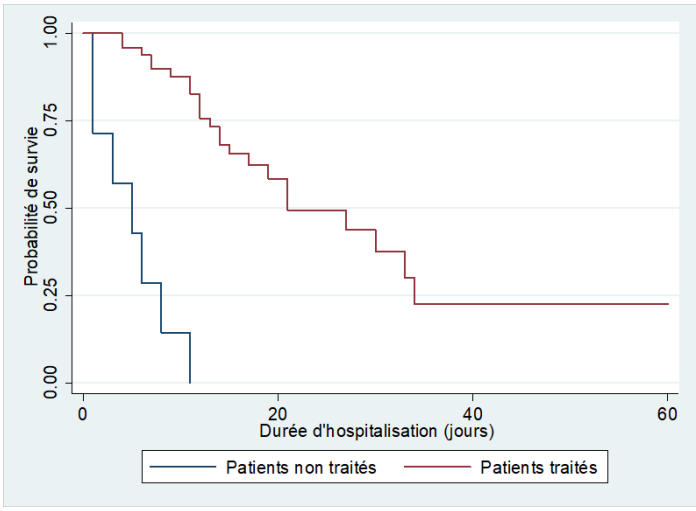


**Figure 2:** Probability of patients survival according to treatment start.

## Discussion

The Service of Infectious Diseases where the study had been conducted has recently been equipped with an archival unit for efficient data management. However, this asset did not prevent from finding out certain files with missing information (duration of hospitalization, diagnosis retained, clinical form of the disease). All these difficulties related to the nature of this study are not new facts, since they have been met by several authors at the level of the sub-region [4,5,9].

However, this study has shed light on the epidemiological situation of neuro-meningeal tuberculosis at the Brazzaville University Hospital while notifying the share of HIV infection in a country with limited resources.

The prevalence of neuro-meningeal tuberculosis is high in the Brazzaville University Hospital, as in France, compared with that found by other authors in the sub-region [9-11]. The methodological differences and socio-cultural habits of the populations studied largely justify the disparities observed in most authors.

Patients were mainly young in our study and in 94.6% of the cases they were under 60 years old. These data are similar to those observed in Africa [9,12]. It is a sexually active layer and mostly exposes itself to the different contributing factors in relation to BK.

The predominance of the female sex in our series is related to the epidemiological data on the feminization of HIV infection as reported by some authors [5,9]. However, this trend is not unanimous since in similar proportions there was a male predominance of neuro-meningeal diseases especially in cases of tuberculosis [13].

The majority of our patients were unemployed and residing in urban areas. Tuberculosis is considered a "disease of poverty", the microbe propagating is preferentially in disadvantaged communities, the dissocialized individuals living in urban areas as reported in the literature [5,14]. In fact, urban areas are densely

populated areas exposed to environmental factors, including aspects of promiscuity, humidity, and lack of ventilation, which are conducive to the transmission of tuberculosis [15].

Patients with neuro-meningeal TB were immunocompromised by HIV in most cases. The low level of CD4 T cells at the meningeal level and the neurotropic nature of HIV, which has become a chronic disease, partly justify this field in these patients [5,13].

The lengthy consultation periods in this study are similar to those described by several African authors [3,5,9]. The ignorance of the disease on the one hand, the cultural considerations associated with poverty largely justify the delay of resorting to the structures of care for these populations not being able to pay a medical consultation [5].

The main symptoms found at admission were fever, behavioral disturbances such as psychomotor agitation, and disturbances of consciousness. These data, classic to previous work carried out in the same service, have also been found in America [5,16-17]. The most common signs found in patients had been the paleness of the mucous membranes in a context of deterioration of the state. Indeed, anemia remains the most striking complication of co-infection with TB-HIV [18]. TNM is one of the meningitis with clear or lymphocyte fluid as reported in our study to significant proportions. The local inflammatory reaction at the meningeal level reflects hyperproteinorachie found in 68.9% of cases with a hypoglycorachie 91.1%. These results corroborate the data mentioned in the literature by several African authors [5,15,19].

The extra-neurological locations were found in 60.7% of cases, they were pulmonary in the majority of cases but also ophthalmological with the presence of tubers of Bouchut in 8.9%. These results are consistent with those obtained by several authors who have conducted studies on the clinical forms of tuberculosis and hypothesizing hematogenous dissemination from a primary focus [5,12,20].

The time elapsed between the diagnosis of neuro-meningeal tuberculosis and the initiation of anti-tuberculosis treatment in our patients seems short. The proximity of the two infectious disease and pneumology services justifies the rapid onset of anti-tuberculosis treatment in the absence of conflict. This period seems short as in Europe [20].

Tuberculosis treatment was administered according to recommendations made by the national program for the control of tuberculosis in Congo in 87.5% of cases [6]. In less proportions, antituberculosis treatment has not been instituted, in connection with the rapid and fatal evolution observed in some patients.

The overall lethality of TN patients in our study was 53.6%. This lethality is less important than that found in a previous study on neuro-meningeal diseases in the same service where death cases were noted in all patients with TNM in the context of immunosuppression to HIV [5]. The result obtained is superimposable to those of the different authors of the subregion [15,21]. The low socio-economic level of our patients for whom the cost of hospital care is out of reach, our working conditions characterized by the limitation of diagnostic and therapeutic means largely justify the high case of fatality observed in this study. The deaths were mainly due to severe anemia, sepsis shock and respiratory distress. The occurrence of death was closely correlated with advanced age as observed by several authors [16,17,21,22], and the lack of start of treatment. The probability of survival decreasing proportionally to the length of hospital stay of these patients.

## Conclusion

The hospital prevalence of neuro-meningeal tuberculosis in the service of Infectious Diseases is high, with a high lethality despite the early treatment instituted. It mostly occurs with people infected with HIV at the AIDS stage regardless of their status in relation to antiretroviral drugs. The factors of poor prognosis identified corroborate those found by other authors and are related to advanced age, the lack of start of treatment. Early detection of HIV infection in the population would reduce the morbidity and mortality associated with this condition.

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