

# Neuro-Meningeal Tuberculosis in Adult Senegalese Patients: Profile and Outcome of Cases Diagnosed at a Referral Service, from 2015 to 2020

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## Abstract

**Background:** Among patients treated for tuberculosis, 2% to 5% have a Central Nervous System (CNS) lesion, and its frequency rises to 10% in HIV-infected patients. Neuro-meningeal tuberculosis (NMT) is responsible for death and severe permanent neurological damage. This poor prognosis requires early diagnosis and rapid initiation of specific treatment. Unfortunately, the great clinical polymorphism and the lack of specificity of radiological and biological signs are frequently responsible for a delay in diagnosis and management. Senegal is one of the African countries where tuberculosis has remained a concern until now. And there are no studies carried out on this subject. **Objective:** The objective of this study was to describe the profile and outcome of Neuro-meningeal tuberculosis (NMT) cases diagnosed at the infectious diseases department (SMIT) of Fann University Hospital in Dakar, (referral service for management of tuberculosis). **Methods:** We carried out a retrospective, descriptive and analytical study, reviewing medical records of adults diagnosed with NMT at the SMIT of Fann Hospital from January 2015 to December 2020. **Results:** We collected 55 cases of NMT. The median age was 38 years [range 16 - 77 years]. The sex ratio (M/F) was 3.23. HIV patients represented 41.82% of cases. A history of tuberculosis was found in 25.5% of cases. The delay in consultation was greater than one month in 60% of patients. Headaches were the most constant reason for consultation (94.55%).

Meningeal signs were present in 94.55% of patients, and consciousness disorders and intracranial hypertension were present in 63.64% and 56.36% respectively. Nerve palsy was found in 38.18%. CSF was clear in 81.64%. GeneXpert MTB/RIF in CSF was performed in 33 patients and was positive in 4 patients. Brain CT was abnormal in 72.09% of cases. Tuberculoma, hydrocephalus and meningeal contrast enhancement were the main lesions. The neuro-meningeal localization was associated with a pulmonary form in 32.7%. The lethality rate was 21.8%; higher in women (46.2% vs 14.3%;  $p = 0.01$ ), in patients with a delay in consultation  $> 1$  month ( $p = 0.03$ ), and in patients who presented with consciousness disorders ( $p = 0.007$ ). **Conclusion:** Despite the availability of the GeneXpert MTB/RIF, diagnosis of NMT remains difficult. Because of its variable clinical expression and the low sensitivity of the GeneXpert MTB/rif in the CSF, it exposes patients to serious complications. Among the factors associated with death, we found consciousness disorders, a long delay in diagnosis.

## Keywords

Neuro-meningeal, Outcome, Profile, Senegal, Tuberculosis

## 1. Introduction

Tuberculosis is a major public health problem, especially in developing countries [1]. It is one of the top 10 causes of death worldwide [2]. Neuro-meningeal involvement is rare but represents one of the most severe forms with high morbidity and mortality. This localization represents 5% - 15% of extra pulmonary tuberculosis [3]. Among tuberculosis cases, 2% to 5% have a CNS lesion and its frequency rises to 10% in HIV-infected patients. The case fatality rate for untreated Neuro-meningeal tuberculosis (NMT) is almost 100% and delay in treatment often leads to permanent neurological damage in more than 50%, despite anti-tuberculosis treatment [4]. Prompt diagnosis is crucial for successful disease management. Unfortunately, the great clinical polymorphism and the lack of specificity of radiological and biological signs, apart from the identification of BK by the nucleic acid amplification test (GeneXpert MTB/RIF) in the cerebral spinal fluid (CSF), make diagnosis difficult and are frequently responsible for a delay in treatment [4]. Senegal is one of the African countries where tuberculosis has remained a concern until now. And there are no studies carried out on this subject. We undertook this study to describe the profile and the outcome of NMT cases diagnosed in the infectious diseases department (SMIT) of the Fann university hospital in Dakar from 2015 to 2020.

## 2. Methods

We carried out a retrospective, descriptive and analytical study, reviewing medical records of adults diagnosed with neuro-meningeal tuberculosis at the SMIT of Fann Hospital from January 2015 to December 2020. The SMIT is in a region

with a high incidence of tuberculosis in Senegal and serves a population of low socio-economic status in Dakar. Cases were identified by reviewing the database of the hospital's Department of Epidemiology and the discharge registry of the infectious diseases department. We included all cases that met the case definition.

Our cases were defined on the presence of at least one of the following criteria:

- Positive GeneXpert MTB/rif in cerebrospinal fluid (CSF) or,
- Lymphocytic meningitis is associated with another confirmed TB site that has progressed well under antituberculosis treatment.

We excluded patients who had incomplete records, patients under 18 years of age and those who had a final diagnosis other than NMT.

We recorded demographic and clinical information, laboratory results, drug treatment and outcome at discharge from the clinical files and microbiology department records. CSF macroscopic examination, protein and glucose quantification and cell count were performed at the hospital laboratory. HIV status was determined using HIV 1 + 2 ELISA test with a confirmatory immunofluorescent assay.

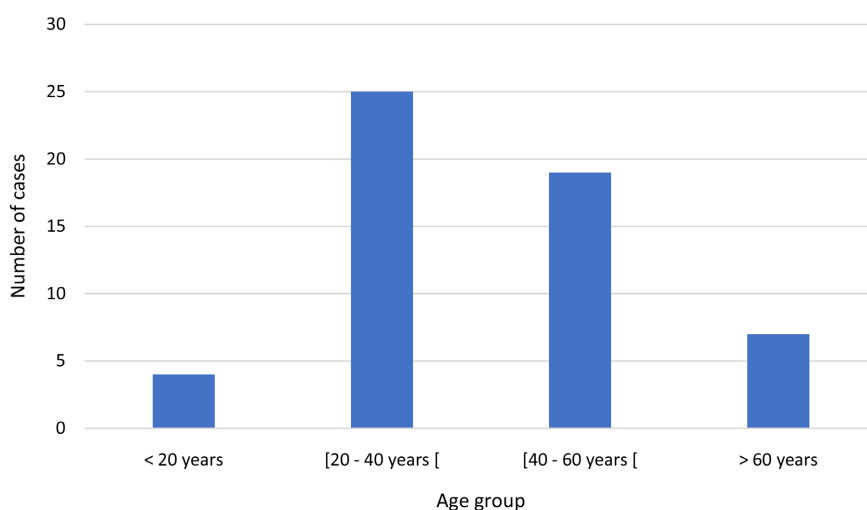
Descriptive statistics were performed for clinical, epidemiological and laboratory features. The statistical analyses were performed with Epi info 7.2 and SPSS V 21. Bivariate analysis was used to look for associations between variables, using Chi2 and Fisher tests. The alpha risk of error was set at 5%.

### 3. Results

Between 2015 and 2020, 5289 patients were admitted to the SMIT. We collected 55 cases of neuro-meningeal tuberculosis, representing a hospital frequency of 1.03% (**Table 1**) and an average of 9 cases per year. The median age was 38 years (range 16 - 77 years). The most affected age group was patients aged between 20 and 40 years (45.45%, n = 25) (**Figure 1**). Patients were predominantly male (76.36) with a sex ratio (M/F) of 3.23. Most of patients (45.45%) live in suburban localities of Dakar. A history of contact was found in 14.5% of cases. HIV- infected patients represented 41.82%. A history of tuberculosis was found in 25.5% of cases (**Table 2**).

**Table 1.** Annual incidence of neuro-meningeal tuberculosis at SMIT of Fann Hospital from 2015 to 2020.

Year	Admitted Patients	NMT Cases	Incidence (%)
2015	1026	2	0.19
2016	991	8	0.8
2017	987	14	1.41
2018	937	18	1.92
2019	938	4	0.42
2020	410	9	2.19
Total	5289	55	1.03



**Figure 1.** Distribution of NMT cases by age group.

**Table 2.** Epidemiological characteristics of NMT at SMIT, Dakar (n = 55).

Epidemiological Characteristics	Frequency (n)	Percentage (%)
<b>Sex</b>		
Male	42	76.36
Female	13	23.64
<b>Origin</b>		
Suburban	25	45.45
Urban	14	25.45
Rural	16	29.09
<b>History of contact</b>		
Yes	08	14.55
No	47	85.45
<b>HIV status</b>		
Positive	23	41.82
Negative	32	58.18
<b>History of TB</b>		
Yes	14	25.46
No	41	74.54

The delay in consultation was greater than one month in 60% of patients. Headache was the most constant reason for consultation (94.55%), Neck stiffness was present for 94.55% of patients, fever was found in 69.09% of cases and vomiting in 60%. Physical examination revealed meningeal signs in 94.55% of cases, consciousness disorders and intracranial hypertension were noted in 63.64% and 56.36% respectively. Nerve palsy was found in 38.18% and pyramid-

al syndrome in 36.36% of cases. Behavioral disorders were presented in 29.09% (Table 3).

Lumbar puncture was performed in 89.09%. The CSF was clear in 81.64%. The mean cytology value was  $312.69 \pm 614.83/\text{mm}^3$ . Thirty-five patients (71.4%) had 100% lymphocytic CSF. High protein level ( $>1 \text{ g/L}$ ) was noted in 77.50%, and 71.40% had hypoglycorachia ( $<0.5 \text{ g/L}$ ). GeneXpert MTB/RIF in CSF was performed in 33 patients and was positive in 4 patients (12.12%); no cases of rifampicin resistance were detected (Table 4). CRP was elevated at 85.45%, the mean value was  $59.19 \pm 58.55 \text{ mg/L}$ .

Brain CT performed in 78.18%, was abnormal in 72.09% of cases. Tuberculoma (27.90%), hydrocephalus (16.27%) and meningeal contrast enhancement (11.62%) were the main lesions. The neuro-meningeal localization was isolated in 61.18%, and in 32.7% it was associated with a pulmonary TB. All patients had been put on anti-tuberculosis treatment (2RHZE/10RH), which had been initiated in 83.64% of cases within a week of hospitalization.

Hyponatremia was the most frequent complication (50.9%). The median hospital stay was 19 days [range 2 - 96 days], and the average length of hospital stay was  $22.75 \text{ days} \pm 18.14 \text{ days}$ . Twelve patients (21.8%) died during hospitalization. There was no association between HIV status and death ( $p = 0.8$ ). The presence of seizures was not statistically significantly associated with death ( $p = 0.46$ ). The Lethality rate was higher in women (46.2% vs. 14.3%;  $p = 0.01$ ), in patients whose delay in consultation was  $>1 \text{ month}$  ( $p = 0.03$ ), and in patients who presented consciousness disorders ( $p = 0.007$ ). We did not find age, HIV status, or the presence of seizures as associated factors of death in our study (Table 5).

**Table 3.** Clinical characteristics of NMT at SMIT, Dakar (n = 55).

Clinical Characteristics	Frequency (n)	Percentage (%)
<b>Delay in admission</b>		
<1 month	22	40.00
>1 month	33	60.00
Headache	52	94.55
Neck stiffness	52	94.55
Fever	38	69.09
Consciousness disorder	35	63.64
Vomiting	33	60.00
Intracranial hypertension	31	56.36
Nerve palsy	21	38.18
Pyramidal syndrome	20	36.36
Behavior disorder	16	29.09
Cerebellar syndrome	12	21.82
Seizures	10	18.18
Associated pulmonary TB	18	32.72

**Table 4.** CSF cytochemistry study in neuro-meningeal tuberculosis cases at SMIT, Fann Hospital (n = 49).

CSF Cytochemistry	Frequency (n)	Percentage (%)
<b>Macroscopic CSF appearance</b>		
Clear	40	81.64
Purulent	9	18.36
<b>Pleiocytosis/mm<sup>3</sup></b>		
<5	11	22.45
[5 - 300[	23	46.90
>300	15	30.61
<b>Predominance</b>		
Lymphocytes	35	71.40
Neutrophiles	2	4.00
variegated	12	24.60
<b>Proteinorachia</b>		
<1 g/l	11	22.50
≥1 g/l	38	77.50
<b>Glycorachia</b>		
<0.5 g/l	35	71.40
≥0.5 g/l	14	28.60
<b>LCS GeneXpert MTB/RIF (n = 33)</b>		
Positive	4	12.12
Negative	29	87.88

**Table 5.** Associated factors with death in neuro-meningeal tuberculosis cases at SMIT, Fann hospital (n = 55).

Associated Factors		Death		P
		Yes, n (%)	No, n (%)	
<b>Sex</b>	Male	6 (14.3)	36 (85.7)	<b>0.01</b>
	Female	6 (46.2)	7 (53.8)	
<b>HIV status</b>	Positive	5 (21.7)	18 (78.3)	<b>0.8</b>
	Negative	7 (22.6)	24 (77.4)	
<b>Delay in admission</b>	>1 month	10(30.3)	23 (69.7)	<b>0.03</b>
	<1 month	2 (9.1)	20 (90.9)	
<b>Glasgow score</b>	[5 - 9[	1 (20.0)	4 (80.0)	<b>0.007</b>
	[9 - 13[	6 (46.2)	7 (53.8)	
	[13 - 14[	0 (0.0)	17 (100)	
<b>Seizures</b>	yes	2 (20.0)	8 (80.0)	<b>0.46</b>
	no	10 (22.2)	35 (77.8)	

## 4. Discussion

In our study, we found a hospital frequency of 1.03% and an annual incidence of 9.16 cases per year. Incidences of neuro-meningeal tuberculosis vary from one series to another [5] [6]. This variability can be explained by the difference between the type of population studied, the conditions under which it was carried out, the study sites and the diagnostic tools used.

Patients were mainly young in our study. These data are similar to those observed in Africa [7] [8] [9]. Indeed, this age group corresponds to the active population, which is the most representative in our countries. The distribution of neuro-meningeal tuberculosis by sex varied according to the different series in the literature. The strong male predominance observed in our study confirms the data in the literature in which male predominance remains classic [5] [6]. However, Ossibibi in Congo in 2020 [6] reported a female predominance (67.9%), while Dollo and al., found in Casablanca in 2017, an equal distribution between men and women [7].

A low rate of contact history was found by several authors [8] [9], like our result, while the prevalence of the disease is high in our regions, this situation could be explained by ignorance of the disease by most of the population, the importance of undiagnosed cases making it difficult to assess the notion of contact. A history of TB was found in 25.4% of cases, this result was like the data found in the literature, according to which a history of tuberculosis is frequently found in subjects with meningitis tuberculosis [6] [10].

The frequency of the association of tuberculosis and HIV infection was found in our study (41.82%), as reported by all authors, particularly the neuro-meningeal localization [6] [7].

The lengthy consultation periods in this study are similar to those described by several African authors [6] [7] [11]. The long delay in consultation may be due to several factors, particularly the clinical polymorphism of the disease, the delay in suspicion of tuberculosis by clinicians, the lack of medical information or the difficulties of access to local medical services in our context.

The main symptoms found at admission headache were fever and consciousness disorder. These data have also been found by several authors [6] [12]. Cranial nerve palsy remains a frequent manifestation of neuro-meningeal tuberculosis and was found in 38.18% of cases in our study. Similar results were found by Amara *et al.* [13]. The extra-neurological locations were common in our cases. They were pulmonary in most of the cases. These results are consistent with those obtained by several authors [6] [7] [9].

NMT is one of meningitis with clear or lymphocyte fluid as reported in our study to significant proportions. The local inflammatory reaction at the meningeal level reflects the hyperproteinorachie found. These results corroborate the data mentioned in the literature by several African authors [6] [7].

GeneXpert MTB/rif in CSF was positive in 12.12%. The detection of *Mycobacterium tuberculosis* by microscopic examination of CSF is an important

means of confirming the diagnosis, but its sensitivity remains low. Thus, the diagnosis of TNM remains difficult and in most cases relies on a range of arguments. This situation tends to delay the diagnosis and exposes patients to the occurrence of complications, which worsens the prognosis of the disease. Brain CT is an important diagnostic tool; however, abnormalities are highly variable. The incidence of hydrocephalus increases with the duration of the disease and decreases with age. It is particularly frequent in children, found in 87% of cases, whereas it is observed in only 12% of adults [14].

Hyponatremia, the most frequent systemic complication, was found in our series. This biological abnormality is responsible for consciousness disorders [15]. The long delay in diagnosis is an associated factor in many series [5] [6], as found in our study. Moreover, we found lethality higher in women (46.2% vs. 14.3%;  $p = 0.01$ ) without explanation.

The SMIT of Fann University Hospital has been equipped with an archival unit for efficient data management. But this asset did not prevent from finding out certain files with missing information. However, this study has shed light on the epidemiological situation of neuro-meningeal tuberculosis at the Fann University Hospital while notifying the share of HIV infection in a country with limited resources.

## 5. Conclusion

Tuberculosis remains a public health problem and neuro-meningeal involvement represents one of the most severe forms. Its highly variable clinical expression and the low sensitivity of the GeneXpert MTB/RIF in the CSF often make diagnosis difficult, thus exposing patients to serious complications. Among the factors associated with death, we find consciousness disorders and long delays in diagnosis.

## Consent

The patients had signed an informed consent form, which is available.

## Conflicts of Interest

We have no conflicts of interest.

## Authors' Contributions

Daouda Thioub, and Papa Latyr Junior Diouf wrote the manuscript with input of Agbogbenkou Tevi Déla-dem Lawson and Viviane Marie Pierre Cisse Diallo.

Ndeye Aissatou Lakhe and Ndeye Fatou Ngom Gueye drafted the manuscript for important intellectual content. Moussa SEYDI and Sylvie Audrey Diop drafted and approved the final version to be published.

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