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Prevalence and Factors Associated with Infectious Meningitis and Meningoencephalitis Related Deaths in People Living with HIV (PLHIV)

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Abstract

Objective: To determine the prevalence of infectious meningitis and meningoencephalitis and to identify factors associated with death in PLHIV at the Infectious and Tropical Disease Clinic located in the FANN University Hospital Centre.

Patients and methods: This was a descriptive and analytical retrospective study conducted from January 1, 2011 through December 31, 2013. It involved all hospitalized PLHIV in the department of infectious diseases of FANN suffering from meningitis and/or encephalitis.

Results: One hundred and thirty-three (133) cases of meningoencephalitis among the 1033 hospitalized PLHIV were collected, which makes 12.9% hospital prevalence. The average age was 42 years ± 10 years and the female gender was predominant. The main general signs were fever (91.7%) and overall health impairment (62.4%). The predominant functional signs were headache (58.6%) and vomiting (43.6%). 28.5% of cases had impaired consciousness and more than 2/3 of the patients had meningeal signs. Nineteen percent of the patients had cranial nerve palsy and 18% had a motor deficit. The main extra neurological signs were cough and dyspnea (57.9%). The lumbar puncture performed in 84.4% of patients showed a clear Cerebro-Spinal Fluid (CSF) in 64.5% of cases and lymphocyte in 1/3 of cases. In 27.1% of patients, the etiology of meningoencephalitis was confirmed and cryptococcosis predominated (16.5%). The lethality was 57% and more than half of the deaths occurred after the 7 days of hospitalization. The presence of headache, impaired consciousness and motor deficit were significantly associated with death.

Conclusion: The high prevalence of infectious meningoencephalitis in PLWHIV and the high lethality associated with this condition justifies the need for early management of HIV infection.

Keywords: Meningitis; Meningoencephalitis; HIV; Fann

Introduction

Infectious meningoencephalitis is the meninge and encephalon inflammation of infectious origin. The spectrum of bacterial, viral, parasitic and fungal etiologies is vast and requires a rigorous diagnostic procedure that should not delay the probabilistic anti-infective treatment of this clinical emergency [1].

Meningitis in PLHIVs is almost always infectious [2] and caused by many factors, some of which are classified as opportunistic infections [3]. In the western world, the incidence has decreased with the introduction of antiretroviral therapy (ART) and the opportunistic infections prevention molecules [4]. However, in Sub-Saharan Africa, it remains to be one of the leading causes of death in HIV patients [4].

In Senegal, few studies have been conducted on the etiology of this pathology, especially among PLWHIVs, which explain why we decided to perform this research, in order to:

Describe the epidemiological, clinical, paraclinical and evolutionary aspects of infectious meningitis and meningoencephalitis in PLWHIV at the Infectious Disease Clinic of the Fann National University Hospital Center.

Identify the factors associated with death.

Patients and Methods

Type of study

This was a retrospective, descriptive and analytical study conducted from January 1, 2011 through December 31, 2013, based on the records of patients living with HIV and hospitalized for meningitis

and/or infectious encephalitis, in the Infectious and Tropical Diseases Department located in the Fann University Hospital Center.

Inclusion criteria

All the HIV patients hospitalized during the study period for infectious meningitis and/or encephalitis. The diagnosis of meningoencephalitis was accepted according to the following hypotheses.

Clinics: Signs of neuromeningeal involvement (headache, meningeal syndrome, coma, convulsions, macroscopic appearance of Cerebro-Spinal Fluid).

Paraclinical: Signs of biological orientation (CSF cytochemistry) and/or bacteriological, viral or fungal confirmation (causal agent detection by direct examination, culture, molecular biology), signs of orientation to brain imaging.

Therapeutic: Good evolution under anti-infectious treatment.

Exclusion criteria

All patients hospitalized for meningitis and/or encephalitis with positive HIV serology with unusable records, particularly patients who died in the beginning of hospitalization without neither paraclinical examinations nor test treatment.

Studied variables

Epidemiological variables (age, sex, HIV profile, backgrounds and field), clinical (symptoms, WHO clinical stage), paraclinical (cytochemistry, bacteriology, culture, cerebrospinal fluid PCR, cerebral CT), therapeutic (anti-retroviral treatment, anti-infective treatment) and evolutionary (healing, death, sequelae).

Data entry and analysis

We used the Epi Info software version 3.5.1 for data entry and analysis. For bivariate analysis, the Pearson Chi-squared and Fischer tests were used to search for factors associated with patient death occurence. A p value<0.05 was used as the level of significance.

Results

Epidemiological aspects

During our study, 133 cases of meningitis and/or encephalitis out of a total of 1,033 HIV-positive patients were collected, representing a hospital prevalence of 12.9%. The average age was 42 ± 10 years and the age group (36-46) was the most represented. The female sex was predominant with a sex ratio (F/M) of 1.18 (Table 1).

Variables	Number	Percentage rate
Age group (years)		
10-36	40	30
36-56	80	60
>56	13	9.7
Marital status		
Married	66	49.6
Unmarried	16	12
Widower	15	11.2
Divorced	22	16.5
Unspecified	14	10.5
Comorbidities		
Alcohol	16	12
Tobacco	21	15.8
Diabetes	3	2.2
Tubercuosis	23	17.3
Tuberculosis contact	4	3
Geographical origin		
Urban	50	37.5
Suburban	51	38.3
Rural	10	7.5
Other country	2	1.5
Unspecified	20	15
Occupation		
Housewife	27	20.3
Merchants	22	16.5
Worker	10	7.5
Official	8	6
Unemployed	2	1.5
Unspecified	64	48.1

Table 1: Distribution of patients by epidemiological aspects.

Clinical aspects

The most common functional signs were headache (58.6%) and vomiting (43.6%). The main general signs found were fever (91.7%) and altered general state of health (62.4%). More than 2/3 of our patients had physical meningeal signs and 28.5% of cases had impaired consciousness. Cough and dyspnea were the most represented extra neurological signs (57.9%) (Figure 1).

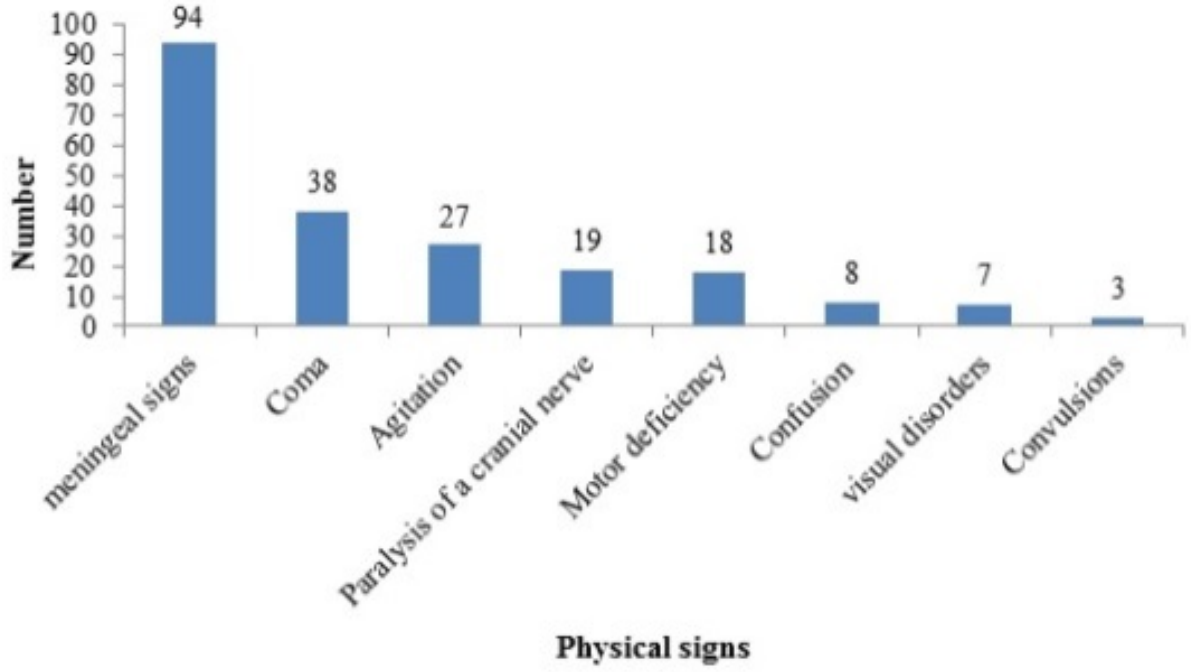

Figure 1: Distribution of patients by physical signs.

Paraclinical aspects

Most patients were infected with HIV-1 (94%). TCD4+lymphocyte counts were performed in 77 patients (58%) and the average rate was 113 cells/mm^3 ± 57.9.

Lumbar puncture was performed in 107 patients (84.4%) and CSF was clear in 69 patients (64.5%) and blurred in 21.5% of cases. The leucocyte average of the abnormal cytology group (≥5 elements) with the specified leukocyte formula is 572 elements ± 2032 with extremes ranging from 6 to 15,000 leukocytes (Table 2).

CSF (n=107)	Number	Percentage
Macroscopy		
Clear fluid	69	64.5
Blurred fluid	23	21.5
Pleocytosis (n=57)		
Lymphocytic	38	35.5
Purulent	12	11.2
Mixed CSF	6	5.6
Chemistry		
Hypoglycorrachia	59	55
Hyperproteinorachia	75	70

Table 2: Distribution of patients according to CSF results.

For 8 Latex cases performed (7.5% of lumbar punction), 4 returned positive with 3 to Pneumococcus, 1 to Streptococcus B. Of 78 direct examinations performed (72.9% of Lumbar punction), 2 returned positive; and the germs found were gram-positive diplococci. The culture was performed in 73 patients and was negative in 100% of cases. GenXpert CSF was performed in 14 patients; and two of them were positive.

Out of 78 direct CSF fungal tests, 11 were positive for Cryptococcus neoformans. The culture carried out on 5.6% of lumbar punction cases, isolated 1 case of Cryptococcus neoformans. Cryptococcal antigen testing, performed on 46.7% of lumbar punction cases, showed 10 positive results.

Blood culture was performed in 31.6% of patients, and a positive result observed in 3% of them including 2 cases with Enterobacter spp, 1 with Flavobacterium spp and 1 with Staphylococcus saprophyticus. The search for mycobacteria, in biological media other than CSF, yielded 1 positive result on 29 samples taken for acid-fast bacilli (AFB) research; against 6 positive results on 19 samples tested for GenXpert.

Of the 25.6% of cases with toxoplasmic serology, 6% had a positive result. Cryptococcal antigenemia was performed in 42.8% of patients and 9.8% had a positive result. Syphilitic serology was performed in 62.4% of patients and a positive result in 4.5% of cases. Only one patient had to benefit from a herpetic serology; and the result returned positive with IgG for Herpes Simplex Virus 1 (HSV1).

Thus, in 27.1% of our patients the etiology was known and confirmed. Neuromeningeal cryptococcosis predominated with a rate of 16.5%. Diagnostic associations have been noted in some patients (1 case of cryptococcosis toxoplasmosis). However, in 72% of patients, microbiology could not confirm the diagnosis (Figure 2).

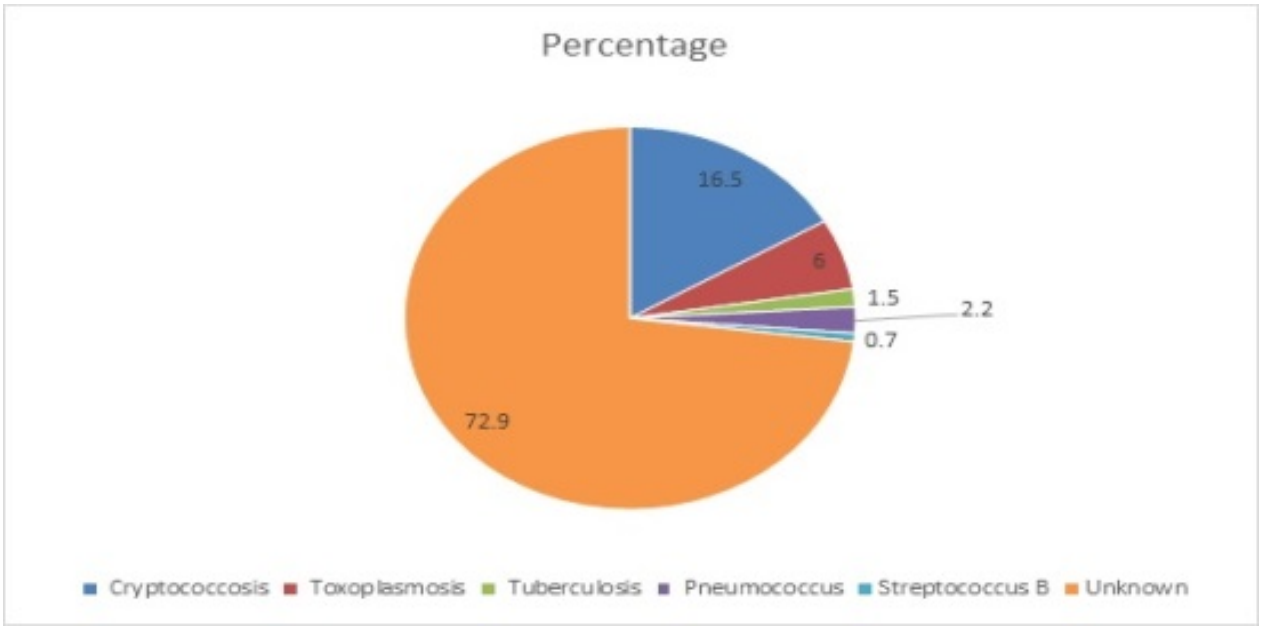

Figure 2: Distribution of patients according to microbiological results.

Brain imaging (Computed Tomograghy: CT, Magnetic Resonnance Imaging: MRI) was performed in 60 patients (45.1%). CT has confirmed on the one hand and sustains on the other hand the diagnosis of 28 cases of meningoencephalitis sometimes associated with an expansive intracranial process. It also diagnosed two ischemic strokes, two ethmoid sinusitis, five cases of cortical atrophy and leukoencephalopathy.

Other examinations have been performed. It consisted of one a case of abdominal CT, four cases of abdominal ultrasound, one case of shock, 1 one case of MRI of the spine: all in favor of tuberculosis; and two cases of Electroencephalogram (EEG) showing cerebral pain.

Therapeutic aspects

The molecules used in the treatment were ceftriaxone alone (77.4%) or combined with other antibiotics (44.6%). It has been associated with gentamicin, metronidazole or both, and vancomycin (1 case). Cotrimoxazole (54.1%), antituberculotic drugs (46%), fluconazole (17.3%) and acyclovir (16.5%). Antiretroviral treatment was unknown in 71% of cases and included 2 Nucleoside Reverse Transcriptase Inhibitors (NRTIs)+1 Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) in 27% of cases.

Evolutionary aspects

Our series lethality was 57.1%. More than half of these deaths occurred after the 7th day of hospitalization (56%).

Factors associated with death (Table 3).

Factors	Death		p
	Yes n (%)	No n (%)	
CSF cytology			
10–100	28 (56)	22 (44)	0.2164
100–1000	20(47.6)	22(52.4)	
CD4 Cells			
<200	39(54.9)	32(45.1)	0,0568
≥ 200	03(30.0)	07(70.0)	
Headache	40(51,3)	38(48.7)	0.0345
Coma	17 (81)	04 (19)	0.0097
Motor deficiency	21(80,8)	05(19.2)	0.004

Table 3: Death-associated factors.

The occurrence of death was predominant in patients with headache (p=0.03), coma-type consciousness disorder (p=0.009) or motor deficit (p=0.004). The depth of immunosuppression (p=0.0568) or hypocytorachia (p=0.2164) were associated with significant lethality but with no statistically significant difference.

Discussion

Limitations

During this retrospective study we encountered some difficulties:

The difficulty of having the exact number of cases of meningoencephalitis due to the loss of some records.

The failure or loss of results of certain paraclinical assessments necessary for diagnosis, such as the CSF examination of cerebral CT, linked to a lack of resources due to a low socio-economic level of patients, certain shortcomings in record keeping and archiving.

The difficulty of collecting comprehensive data on the HIV previously known and managed.

During our study period, the hospital prevalence of meningitis and infectious encephalitis was 12.9%. This prevalence, though high, is lower than those found in other studies conducted in Africa (Hakim in Zimbabwe: 85% in 10 months [5], Kanyamahanga in Rwanda: 17.4% in 5 years [6]. This high prevalence could be explained by the delayed diagnosis and treatment of HIV infection in Africa; mainly during the stage of severe immunosuppression with the occurrence of opportunistic infections (meningoencephalitis: circumstance of discovery of HIV in 54.1% of patients). In fact, for some of them, the occurrence depends on the level of immunosuppression (the average CD4 level is low in our patients<200 or 112.8/mm^3). On the other hand, this may be related to the resurgence of tuberculosis, which is the first opportunistic HIV infection in developing countries [7].

The average age of our patients was 42 ± 10 years and the age group (36-46) was the most represented. Our results are quite similar to those of Evelyne Aka Anghui Diarra from the University Hospital of Cocody (Abidjan) [8] and Soumaré who found an average age of 40.5 years and 40.7 years respectively [9]. This may be related, on the one hand to the epidemiology of HIV/AIDS (the highest prevalence is noted between 40-49 years [10], and on the other hand, to the natural history of HIV infection with the occurrence of these opportunistic infections at stage 4 (WHO classification) 10 years after infection [11].

All the classic functional signs of meningoencephalitis such as headaches, vomiting and bowel movement disorders have been found.

Headache was present in 58.6% of patients. This rate is lower than that of Soumaré, Ouattara and Ganien who found respectively 80%, 89.5%, 80.4% [9,12,13]. Vomiting (43.6%) and bowel movement disorders (10.5%) were lower than Ouattara's results who respectively obtained 62.7% and 51.1% [12]. The meningeal syndrome was present in 70.7% of the patients which is comparable to Soumaré's results (74%) [9]. However, they are lower than those of Ouattara [12] and Ganiem [13] who respectively found 83.1% and 91.5%.

Obnubilation and coma were observed in 44.4% of cases, which is similar to the result of Ganiem (44.7%) [13], but higher compared to that of Soumaré (28%) [9]. However, the rate found by Ouattara is much higher (72.2%) [12].

Agitation and general convulsions were found in 13.5% of patients. Soumaré found a lower rate (09%) while Ouattara's result was twice as high (33%) [9-12].

CSF was clear in most cases (64.5%). Soumaré found a similar result, but at a lower rate (51.7%) [9]. In contrast, Ouattara observed a majority of purulent CSF (80.5%) [12]. This is consistent with the literature data. This is the most common clinical situation; in fact, during HIV immunosuppression, the main etiologies of meningoencephalitis are clear CSF [14]. With regards to the CSF analysis: hypercellularity was found in 57 patients (53.3%). The CSF was lymphocytic in 38 patients, meaning 35.5%, purulent in 12 patients (11,2%). On average, it had 572 elements ± 2032. This is consistent with Ganien's results with a lymphocyte majority (60%) but less rich in cells (18 elements/ml) [13].

A median glycorachia of 0.41 g/l with extremes of 0.05 and 2.93 was observed and hypoglycorachia was noted in 59 patients, meaning 64.1%. A median protein concentration of 1.21 g/l with extremes of 0.01 and 10 was found. A hyperproteinorachia was observed in 75 patients or 82.4% of which 24.2% had a value between 0.5 and 1 g/l; and 58.2% a value>1 g/l. This is comparable to Ouattara's results who studied bacterial and cryptococc al meningitis: hyperproteinorachia at 1.3 g/l and hypoglycorachia at 0.16 g/l for its entire series [12]. In the same way, Hakim found in his series a hypoglycorachia in 5.8% of the cases and a hyperproteinorachia in 79.9% of the cases [5]. These results of CSF chemistry could be explained by our study etiology trend with a majority of tuberculosis and cryptococcal neuromeningeal and some pyogenic meningitis.

In our series cryptococcosis was the main etiology (16.5%) corroborating Soumaré's studies in Senegal (63%) [9] and Ganiem in Indonesia (30%) [13]. In 73% of cases, the etiology was not found, a rate clearly above that of Soumaré (26%) [9]. These results are related to the poor technical platforms found in our regions, particularly the inaccessibility to new, sensitive detection techniques of micro-organisms such as molecular biology, culture on specific media among others. It should also be noted that in this group of 98 patients (73%) whose etiology was not found.

The diagnosis of neuromeningeal tuberculosis was retained in 34 patients on the basis of indirect hypotheses: epidemiological (notion of contagion, antecedents), clinical (evening fever in the long term, altered general state of health, other tuberculous foci existence), biological
(lymphocytic meningitis, hyperproteinorachia) and therapeutic (impro vement under antituberculous treatment).

For another group of nine patients, the etiology was herpetic based on clinical arguments (herpes lesions), paraclinical (lymphocytic CSF with normoglycorachia) and therapeutic (improvement with acyclovir).

And for the remaining 55 patients, the CSF cytochemistry allowed to classify them: 06 cases of purulent CSF, 03 cases of variegated CSF, 03 other cases of lymphocyte CSF suspected of neuromeningeal listeriosis (therapeutic argument), 08 cases of lymphocytic CSF and finally 35 unclassifiable cases. However, among our patients, these etiologies were found in diagnostic association (either tuberculosis with toxoplasmosis or purulent meningitis) in some cases.

We found a lethality of about 57.1%. The same data is found in meningitis and/or encephalitis literature in sub-Saharan Africa, with a lethality standing between 25 and 68% [4]. The poor technical platform, in terms of the diagnostic and therapeutic tools and the delay in screening for HIV infection could explain this fact. Factors associated with death were headache, impaired consciousness, and motor deficit. Awareness disorders have been identified by Zohreh as a factor associated with death from TB meningoencephalitis [14]. These signs associated with intracranial hypertension, constitute elements of poor prognosis of infectious meningoencephalitis.

Conclusion

This study shows the high prevalence and poor prognosis of infectious meningitis and meningoencephalitis in PLWHIV in our regions. It also highlights the etiological diagnosis difficulty found in these conditions which consequently makes therapeutic management difficult.

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