

# Etiologies and associated Factors Death among People living with the Human Immunodeficiency Virus (PLHIV) Hospitalized for Febrile Consciousness Disorders in the Infectious and Tropical Diseases Department of the Donka National Hospital, Guinea.

## ABSTRACT :

**Introduction** :Central nervous system (CNS) damage is common during human immunodeficiency virus (HIV) infection and occur in cases of immunosuppression, which leads to altered consciousness. The objective of this work was to identify the etiologies and factors associated with the death of PLHIV hospitalized for febrile consciousness disorders in the infectious and tropical diseases department from Donka National Hospital.

**Methodology**:This was a retrospective study of descriptive and analytical type over five (5) years in the infectious and tropical diseases department of the Donka National Hospital. Included in this study were PLHIV under treatment antiretroviral (ART) or not, aged over 15, hospitalized in the infectious diseases department of Donka National Hospital. for febrile consciousness disorders or those who developed it during the study period.

The parameters studied were sociodemographic characteristics, clinical picture, clinical staging of HIV/Acquired Immuno-Deficiency Syndrome (AIDS) according to the World Health Organization (WHO).

Factors associated with deaths were searched from logistic regression in multivariate analysis and all variables with a value of  $P < 0.05$  were considered statistically significant

**Results** :Two hundred and five out of five hundred and thirty-four (205/534) files of PLHIV, hospitalized for febrile consciousness disorders were sampled and enrolled for this study, i.e. a prevalence of 38.39%. The average age of the patients was  $42.28 \pm 12.54$  years with a sex ratio of 0.97. Cerebral toxoplasmosis was the most common etiology. Severe immunosuppression was one of the factors statistically associated with death. **Conclusion** :Febrile consciousness disorders remain very common, with multiple etiologies in PLHIV. The CD4 count  $\leq 200$  cells/mm<sup>3</sup>, the depth of the coma and the absence of antiretroviral treatment were the factors associated with death.

Keywords: Consciousness Disorders, Fever, Pvhiv, Etiologies, Death, Donka, Guinea.

## Introduction :

Febrile consciousness disorders are defined as any alteration of alertness accompanied by a temperature above 38°C of central origin or not. They can range from a state of simple

obtundation or stupor to the stage of coma [1]. Human immunodeficiency virus is an infection caused by a retrovirus that attacks the body's immune system by destroying it, thus weakening the effectiveness of the patient's immune system [2]. Central nervous system (CNS) damage is common in people infected with HIV and occurs often in cases of immunosuppression, which leads to altered consciousness [3,4]. Cerebral toxoplasmosis still remains the most frequently encountered opportunistic infection in AIDS, followed by neuromeningeal cryptococcosis and bacterial infections which are responsible for impaired consciousness [3,5].

Most studies around the world show that the main factors associated with death among PLHIV were late diagnosis of HIV, non-compliance ARV treatment (ART), ART failure, the absence of ART, a CD4 count  $\leq 200$  cells/ $\mu$ L, a Glasgow score less than 12 and the presence of opportunistic infections linked to HIV [6]. According to the United Nations HIV/AIDS program (UNAIDS) in 2023, HIV-related deaths were 13,000 in the USA; 28,500 in Europe and 195,000 in Africa [7].

A study carried out in Germany found that people living with HIV (PvHIV) represented 10 to 30% of all adults admitted with disorders of consciousness [8]. A study in Nigeria also found similar results [9]. In Uganda, a study carried out in 2022 found that the absence of ART and the Glasgow score less than 12 represented 45% and 30% respectively of the factors associated with death [10]. In Ukraine study carried out and published in 2014 showed that late diagnosis of HIV and failure ART represented 42% and 24% of the factors associated with death, respectively [11].

However, in Guinea, little data exists on this subject, it is therefore in this spirit that we initiated this study with the aim of goals:

#### **General :**

Identify the etiologies and factors associated with the death of HIV-positive patients hospitalized for febrile disorders of consciousness in the infectious and tropical diseases department of DONKA University Hospital.

#### **Specific:**

Determine the prevalence of febrile consciousness disorders among PLHIV hospitalized at the department of Infectious and Tropical Diseases of the Donka National Hospital, Guinea.

Describe socio-demographic characteristics

Identify the most frequently found etiologies

Highlight the factors associated with death

## **1-Materials and methods:**

This was a retrospective study of descriptive and analytical type lasting 05 years from July 1, 2018 to June 30, 2024, carried out in the infectious and tropical diseases department of the Donka national hospital. It is the reference service in the management of HIV infection in adults in Guinea.

Were included in this work **PLHIV files** on ARV or not, **male or female**, aged over 15 years, hospitalized in the infectious diseases department for febrile consciousness disorders or those who developed it during our study period.

For data collection, we carried out an exhaustive recruitment of all patient files meeting the selection criteria during the period considered.

The parameters studied were: sociodemographic characteristics, clinical picture, clinical staging of HIV/AIDS according to WHO, etiologies and factors associated with death in hospitalized patients.

#### **Definition of variables:**

**Age:** number of years lived by the person until the day of hospitalization. Patients were grouped by age group of 10 years.

**Gender:** permanent physical character of a person making it possible to distinguish male and female individuals but also to determine the sex ratio.

#### **Marital status :**

**Married :** two people united by a matrimonial bond.

**Bachelor :** person who is not married.

**Divorce :** a person whose marriage has been legally dissolved.

**Widower:** person whose spouse has died.

#### **Socio-professional layer:**

This is the professional activity of the patient and is classified into:

**Formal sector:** set of official activities, recognized by the state with monthly remuneration.

**Informal sector:** all activities producing goods and services which escape the gaze or regulation of the state. (Driver, worker, merchant/trader, hairdresser, seamstress, farmer).

**Housewife:** woman who runs a house, takes care of the household.

**Pupil/student:** people who receive education in a pre-university school, university or professional establishment.

**Unemployed:**all people who do not have a job.

**School level:**it designates the highest level of education attained by the patient: Low: person whose level of education is limited to primary school.

Secondary: person whose level of education is between the end of primary school and the start of university.

Higher: person whose level of education is university.

**Etiologies:**

**Cerebral toxoplasmosis:**Opportunistic parasitic infection due to *Toxoplasma gondii* which occurs when the CD4 count is less than 200 cells. Diagnosis is made from medical imaging CT/MRI of the brain or PCR *Toxoplasma gondii* in the CSF / more or less PCR in the plasma or from clinical improvement by a 15-day antitoxoplasmic test treatment.

**Tuberculosis:**Gen-expert positivity in cerebrospinal fluid.

Gen-Expert: tuberculosis diagnostic tool, rapid, sensitive and specific for *Mycobacterium tuberculosis* with a sensitivity of 89% and a specificity of 91%. It is a real-time molecular biology test.

**Cryptococcosis:**opportunistic fungal infection appearing at the AIDS stage.

CRAG in CSF: qualitative and semi-quantitative detection of CSF antigens ***Cryptococcus neoformans*** in the cerebrospinal fluid (CSF)

**Neuromalaria:**Thick drop positive for *Plasmodium falciparum* + Coma

**Bacterial meningoenzephalitis:**cloudy or purulent cerebrospinal fluid with or without identification of the bacterial germ responsible.

**Viral meningoenzephalitis:** Clear CSF with or without isolation of the virus responsible by PCR

**Brain abscess:** focal suppuration of infectious origin developed within the brain parenchyma and appears regardless of the CD4 count. The diagnosis is made by brain imaging which highlights multiple foci of abscesses.

**CMV enzephalitis:**occurs if CD4 count is less than 50 cells

**Syphilitic enzephalitis:**non-specific neuropsychological disorders. Syphilitic serology and VDRL positivity in the cerebrospinal fluid allow the diagnosis to be made.

**Lymphomas:**headaches, vomiting, physical asthenia, mood changes are non-specific. Brain magnetic resonance imaging (MRI) and neurosurgical biopsy help confirm the diagnosis

**HIV encephalitis:** progressive deterioration of cognitive function in an HIV+ patient not on antiretroviral treatment or on antiretroviral treatment but with failure of cerebral virological control. MRI and cerebral lumbar puncture help eliminate other differential diagnoses.

Qualitative variables were presented as proportions and quantitative variables as means and standard deviation. The student test was used for quantitative variables and the chi-square test was used for qualitative variables with a significance threshold of 5%. Multivariate logistic regression was used to test the association of the different factors identified with the occurrence of death for variables with P values < 5%.

Data entry and analysis were carried out using EPI data software in version 3.1 and SPSS software in version 21, then processed by Microsoft Word and Excel 2013 software.

## **2-Results:**

During the study period, 205/534 PLHIV hospitalized for febrile consciousness disorders were included, i.e. a prevalence of 38.39%.

The average age of the patients was  $42.28 \pm 12.54$  years [18-85 years] with a slight female predominance, i.e. a sex ratio of 0.97. The informal sector represented almost 43% (88/205) of patients and almost 2/3 (69.96) of patients had a low level of education and more than half (62.44%) of patients were married. . (Table 1)

Weight loss (66.34%) and cough (40%) were the most frequently found signs (Table 2).

Almost all (97.07%) of the patients had HIV type 1

More than 94% (180/205) of patients were in the severe immunosuppression stage (Table 3).

Only 6.82% (14/205) of patients were able to perform a brain scan and no magnetic resonance imaging was done (Table 4).

Cerebral Toxoplasmosis 73/205 (35.61%) and Neuromeningeal Cryptococcosis 45/205 (21.95%) were the most frequently found etiologies (Table 5).

Only 1/3 or 33.66% (69/205) were on ART during the study period.

More than 5/6 (83.90%) of our patients died

The depth of coma, the absence of antiretroviral treatment and a CD4 count  $\leq 200$  cells/mm<sup>3</sup> were the factors associated with death in multivariate analysis. (Table 6).

## **3-Discussion:**

This was a retrospective descriptive and analytical study on the etiologies and factors associated with the death of PvHIV hospitalized for febrile consciousness disorders. Despite the retrospective

and monocentric nature, this study allowed us to identify the etiologies and factors associated with the death of PLHIV hospitalized for febrile consciousness disorders in the infectious and tropical diseases department from Donka National Hospital.

The prevalence in this study is comparable to that of Adoukonou et al in Benin in 2014 who found 38.1% [12]. On the other hand, El Fane et al in Morocco in 2018 [13] found a significantly lower prevalence of 11%.

This high prevalence in our series could be explained by the fact that the majority of patients consult the late phase of HIV infection where opportunistic brain infections are very common.

The average age of our patients is close to that of Roland [3] in 2016 in Congo Brazaville who found 41.10 years and higher than those of Adoukonou [43] in Benin in 2014 and EL Fane [13] in Morocco in 2018 who reported 38 and 39 years respectively.

This slight female predominance is similar to those of Franck et al [14] in Ethiopia in 2019 and Gunda et al [15] in Tanzania in 2016 with 62.1% and 61.85% respectively.

The informal sector most affected in this work was similar to that of Ossibi I et al [3] which had brought in 40%.

In this study, married couples were the most represented. The same observation was reported by Mbula et al [16] in 2020 in the Democratic Republic of Congo with 63%.

Weight loss, the most common symptom found in this study, was also reported by Zannou et al in Benin in 2004 [17].

HIV type 1 was found in almost all patients. This observation is similar to those of Traoré et al [18] in 2014 in Mali.

The majority of our patients had a CD4 count below 200 cells/mm<sup>3</sup>. This result is higher than that of Karfo et al [19] in Burkina in 2018 who reported 78% of patients with a CD4 count below 200 cells/mm<sup>3</sup>.

This could be due to the fact that most of our patients consult at a late stage of HIV infection.

Toxoplasmosis, neuromeningeal cryptococcosis and tuberculosis were the most frequently found etiologies.

Concerning the etiologies, similar results were reported by Rolland OIB et al in 2016 in Congo [3].

This is consistent with current literature data which states that toxoplasmosis is the first opportunistic infection of the central nervous system during AIDS [5,20]

Compared to ART-naïve patients, our finding is different from that of Fall et al in Dakar in 2017 [21] who found that less than 10% of patients were naive.

This result could be explained by the fact that the majority of our patients were unaware of their serological status and were therefore not on antiretroviral treatment.

The high case fatality rate in this study is superimposable to those of Rolland et al [3] in 2016 with 83.2% and lower than those of Karfo et al in Burkina in 2018 [19] who reported 44.1% deaths.

This observation could be explained by the fact that the patients were treated at a late stage of HIV infection.

Factors associated with death in this study were similar to those of Chelli J et al in Tunisia, Mbondé AA et al in 2022 in Uganda, Traoré S in 2021 in Mali and Pang W et al in 2018 in China [6,10,22,23] and different from those of Rolland OIB et al [3] in 2016 in Brazzaville who reported that neuro-meningeal tuberculosis and anemia were significantly associated with death.

This result could be explained by the fact that HIV-positive patients not on antiretroviral treatment can rapidly progress towards severe immunosuppression (CD4 rate  $\leq$  200 cells/mm<sup>3</sup>) and therefore become very susceptible to opportunistic brain infections with risk of brain disorders, consciousness and subsequent death.

## **Conclusion :**

Febrile consciousness disorders among hospitalized PLHIV remain frequent in the infectious and tropical diseases department of the Donka National Hospital and toxoplasmosis was the most common etiology. The depth of the coma, severe immunosuppression and the absence of antiretroviral treatment were the factors associated with death.

Screening and early treatment of HIV infection would help reverse this trend.

## **Recommendations:**

Information, education and communication campaigns on HIV infection for the population and health personnel in order to carry out early detection and adequate treatment through ART.

## **Warning (artificial intelligence):**

No generative AI technologies such as large language models (ChatGPT, COPILOT, etc.) and text-to-image generators were used in the writing or editing of this manuscript.

**Consent :** Not applicable.

**The anonymity and confidentiality of patients were respected.**

**Ethical approval:**

The study protocol was approved by the ethics committee of the Faculty of Health Sciences and Technologies of the Gamal Abdel Nasser University of Conakry.

**Conflict of interest:**The authors have declared that no conflict of interest exists.

## Paintings

**Table 1:** Distribution according to socio-demographic characteristics of 205 HIV-positive patients hospitalized for febrile consciousness disorders from 2018 to 2023 in the infectious and tropical diseases department of Donka University Hospital, Guinea

<b>Variables</b>	<b>Effective (n=205)</b>	<b>Percentage (%)</b>
Age		
41-50 years old	63	30.73
Sex		
Women	104	50.73
Marital status		
Married	128	62.44
Others	77	37.56
Educational level		
Weak	143	69.76
Others	62	30.24
Occupation		
Informal sector	88	42.93
Others	117	57.07
Residence		
Conakry	121	59.02
Others	84	40.98

Average age: 42.28 ( $\pm$  12.54) years with extremes of 18 and 85 years

**Table 2:** Distribution according to signs of the 205 HIV-positive patients hospitalized for febrile consciousness disorders from 2018 to 2023 in the infectious and tropical diseases department of Donka University Hospital, Guinea

<b>Signs</b>	<b>Frequency</b>	<b>Percentage</b>
<b>Weight loss</b>	<b>136</b>	<b>66.34</b>
Coma stage 1	128	62.44
Cough	82	40.00
Physical asthenia	79	38.54
Vomiting	73	35.61
Diarrhea	60	29.27
Coma stage 2	56	22.44
Hemiparesis	40	19.51
Psychomotor agitation	30	14.63
Coma stage 3	21	10.24
Chest pain	15	7.32
Dysphagia	15	7.32
Abdominal pain	8	3.9
Dyspnea	6	2.93

**Table 3:** Distribution according to the immuno-virological status of HIV-positive patients hospitalized for febrile consciousness disorders from 2018 to 2023 in the infectious and tropical diseases department of Donka University Hospital, Guinea

<b>Immuno-virological assessment</b>	<b>Frequency</b>	<b>Percentage</b>
Viral Load (n=45)		
Detectable	42	20.48
Undetectable	3	3.41
CD4 rate (n=191)		
<b>Less than 200 cells per mm<sup>3</sup></b>	<b>180</b>	<b>94.24</b>
200-350 cells per mm <sup>3</sup>	7	3.66
350-500 cells per mm <sup>3</sup>	4	2.10

**Table 4:** Distribution according to diagnostic confirmation examinations of HIV-positive patients hospitalized for febrile consciousness disorders from 2018 to 2023 in the infectious and tropical diseases department of Donka University Hospital, Guinea

<b>Diagnostic confirmation examinations</b>	<b>Frequency</b>	<b>Percentage</b>
<b>GE(DP) /TDR (n=204)</b>		
Negative	191	93.63
Positive	13	6.37
<b>CRAG(n=195)</b>		
<b>Negative</b>	150	76.92
Positive	45	23.08
<b>Gen-expert (n=199)</b>		
<b>Negative</b>	151	77.44
Positive	44	22.56
<b>Brain scan (14)</b>		
Abnormal	11	78.57
Normal	3	21.43

**Table 5:** Distribution according to the main diagnosis of HIV-positive patients hospitalized for febrile consciousness disorders from 2018 to 2023 in the infectious and tropical diseases department of Donka University Hospital, Guinea

<b>Main diagnosis:</b>	<b>Numbers (N=205)</b>	<b>Percentage</b>
Toxoplasmosis	73	35.61
Neuromeningeal cryptococcosis	45	21.95
Tuberculosis	44	21.47
Bacterial meningoenzephalitis	28	13.66
Severe malaria	13	6.34
None	2	0.97

**Table 6:** Distribution of HIV patients hospitalized for febrile consciousness disorders in the infectious and tropical diseases department of the Donka University Hospital of Guinea according to factors associated with death in multivariate analysis.

<b>Associated factors</b>	<b>Odds Ratio</b>	<b>Confidence interval</b>	<b>P-value</b>
<b>Coma</b>	6	1.77-17.49	0.003
<b>CD4 rate</b>			
[200-500 cells]	3.54	1.06-14.56	0.7
≤ 200 cells/mm <sup>3</sup>	6.33	1.72-29.0	0.007
<b>Anemia</b>			
Yes/no	0.91	0.005-1.513	0.095
<b>Creatininemia</b>			
Low	0.273	0.023-3.291	0.306
High	14.15	1,478-5,495	0.072
<b>ARV treatment</b>			
Yes/no	0.02	1.74-19.17	0.004

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