

## Immunovirological Profile of HIV Patients with Sepsis in the Infectious Diseases Ward at the Institut des Maladies Infectieuses Professeur Daniel GAHOUMA in Libreville

Manomba Boulingui C<sup>1,2\*</sup>, Ntsame Owono MM<sup>1,2</sup>, Essomeyo Ngui Mebale M<sup>2</sup>, Sibi Matotou R<sup>3</sup>, Mayandza C<sup>3</sup>, Moutombi Ditombi BC<sup>3</sup> and Kombila UD<sup>2</sup>

<sup>1</sup>Infectious Diseases Ward, Institute of Infectious Diseases Professor Daniel Gahouma.

<sup>2</sup>Department of Medicine, Faculty of Medicine, Université des Sciences de la Santé, Owendo, Gabon.

<sup>3</sup>Department of Parasitology Mycology, Tropical Medicine, Faculty of Medicine, Université des Sciences de la Santé, Owendo, Gabon.

### Corresponding Author Information

Manomba Boulingui Charleine

Department of Medicine, Faculty of Medicine, Université des Sciences de la Santé, Owendo, Gabon USS Libreville, Gabon

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### ABSTRACT

**Background:** HIV infection is the main comorbidity of patients hospitalized for sepsis in infectious disease departments in sub-Saharan Africa. The aim of this study is therefore to describe these clinical and immunovirological characteristics in HIV-positive patients with sepsis in Libreville.

**Method:** This retrospective cohort study included 105 HIV-positive patients hospitalized for sepsis (Sepsis-3 criteria) in the infectious diseases ward of the Institut de Maladies Infectieuses Professeur Daniel in Libreville. The immunovirological profile was characterized by: HIV type, WHO stage (1-4), CD4 lymphocyte count (cells/mm<sup>3</sup>), viral load (log copies/mL), antiretroviral status, and circumstances of screening. Opportunistic infections were the only focus of the study. A CD4 quartile analysis was performed. Chi-square, Mann-Whitney U, and Spearman correlation tests were used.

**Results:** HIV was present in 68.2% of the 154 patients with sepsis. Antiretroviral (ARV) coverage was only 31.4%. Immunosuppression was severe: median CD4 count 145 cells/mm<sup>3</sup> (IQR: 79-255), 64.8% with CD4 count < 200 cells/mm<sup>3</sup>, and 46.7% at WHO stages 3-4. The median viral load was 5.16 log copies/mL, with 94.3% of patients having viremia ≥ 1,000 copies/mL. CD4 count was strongly correlated with WHO stage (r = - 0.447; p < 0.0001) and opportunistic infections (7% at stage 1 vs. 92% at stage 3). The circumstances of screening were primarily symptomatic (weight loss 17.1%, cough and fever 10.5%); only 12.4% underwent voluntary screening. Neither CD4 count, viral load, nor antiretroviral status were associated with in-hospital mortality (all p > 0.14).

**Conclusion:** The lack of association between CD4 and hospital mortality suggests that the immediate prognosis of sepsis is determined more by microbial virulence than by the underlying chronic immunosuppression.

### KEYWORDS

HIV, CD4, Viral load, Sepsis, Libreville.

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## Introduction

Human immunodeficiency virus infection remains a major public health challenge, particularly in Saharan Africa is home to more than 67% of the world's people living with HIV approximately 25.6 million people, according to the latest estimates from UNAIDS [1]. The progress made through expanded access to antiretroviral (ARV) treatments has led to a significant improvement in survival rates and a reduction in morbidity associated with opportunistic infections [2]. However, despite these advances, serious infectious complications, particularly sepsis, continue to be a major cause of hospitalization and mortality among HIV-infected patients, especially in resource-limited settings [3].

Sepsis, defined as life-threatening organ dysfunction resulting from an inappropriate host response to infection, is a common and severe medical emergency [4]. In patients living with HIV, the development of sepsis is often exacerbated by advanced immunosuppression, characterized by low CD4 cell counts and high viral loads, indicating inadequate control of viral replication [5]. Furthermore, the clinical stage as defined by the World Health Organization (WHO) reflects the progression of the disease and remains an important indicator of the risk of severe infectious complications [1]. Access to antiretroviral therapy and adherence to treatment also play a key role in preventing these complications by promoting immune recovery and viral suppression [2].

In sub-Saharan Africa, several studies have shown that HIV patients admitted for sepsis frequently have poor immunovirological profiles, linked to delayed diagnosis, late initiation of antiretroviral therapy, and difficulties accessing care [3,5]. The circumstances surrounding HIV testing whether it is an opportunistic diagnosis during hospitalization or voluntary testing also play a key role in determining the stage of the disease at the time of treatment [6]. In Gabon, although progress has been made in HIV testing and care, specific data on the immunovirological profile of patients with sepsis remain limited, particularly in hospital settings. In this context, analyzing the immunovirological profile of patients living with HIV who are hospitalized for sepsis by assessing the WHO stage, CD4 count, viral load, antiretroviral therapy (ART) coverage, and testing circumstances is essential for better understanding the factors that determine disease severity and guiding treatment strategies. The aim of this study is therefore to describe these clinical and immunovirological characteristics in HIV-positive patients with sepsis in Libreville, Gabon, in order to help improve care and reduce sepsis-related mortality in this population.

## Methodology

### Study design and setting

This was a retrospective, single-center cohort study conducted from October 2024 to December 2025 in the Infectious Diseases Ward, at the Institut des Maladies Infectieuses Professeur Daniel GAHOUMA in Owendo, Gabon. Of the 154 adult patients (aged  $\geq 18$  years) hospitalized for sepsis, this analysis focuses on the 105 patients (68.2%) whose HIV-positive status was known at

admission. The diagnosis of sepsis was made according to the Sepsis-3 criteria (organ dysfunction associated with a dysregulated response to infection, SOFA score  $\geq 2$ ) [7].

### Collection of clinical and immunovirological data

For each HIV patient, the following variables were systematically collected from the medical record: (i) HIV type (1 or 2); (ii) ART status at admission (yes/no); (iii) WHO clinical stage (1 to 4); (iv) CD4 lymphocyte count (cells/mm<sup>3</sup>); (v) viral load in copies/mL and in log<sub>10</sub>; (vi) circumstances of HIV testing (initial reason leading to diagnosis); (vii) presence of opportunistic infections or HIV-related intercurrent illnesses; (viii) Xpert MTB/RIF test result when available. Biological data (complete blood count, laboratory chemistry), microbiological data (blood cultures, pathogen identification, and antibiotic susceptibility testing), and hospital discharge status were also collected.

### Operational definitions

Severe immunosuppression was defined as a CD4 count  $< 200$  cells/mm<sup>3</sup>. A CD4 count  $< 50$  cells/mm<sup>3</sup> corresponded to advanced AIDS. Viral suppression was defined as a viral load  $< 1,000$  copies/mL (log  $< 3$ ). Opportunistic infections were classified according to WHO criteria. Late diagnosis was defined as a case in which HIV was diagnosed following the presentation of clinical symptoms (as opposed to voluntary or routine screening). The CD4 quartile analysis was performed on the entire HIV cohort : Q1 (5-79 cell/mm<sup>3</sup>), Q2 (80-145), Q3 (150-255), Q4 (261-566)..

### Statistical analysis

Qualitative variables are expressed as counts and percentages. Quantitative variables are expressed as the median and interquartile range (IQR). Comparisons were performed using the chi-square test (or Fisher's exact test) and the Mann-Whitney test. Correlations were analyzed using Spearman's rank correlation coefficient. Analyses were conducted using Python 3.11. The significance threshold was  $p < 0.05$ .

### Ethical considerations

This study is part of the epidemiological and clinical surveillance activities conducted by the Center for Research on Infectious Pathogens and Associated Diseases (CREIPA), in collaboration with the National Program for the Control of HIV and STIs. Ethical approval was granted by the Ministry of Health. Administrative authorization was obtained from the medical director of the Institut Professeur Daniel GAHOUMA, and the head of the Infectious Diseases Department. A unique anonymous identifier was assigned to each patient, and all data were processed in accordance with the principles set forth in the Declaration of Helsinki.

## Results

### General Characteristics of the cohort

HIV was detected in 105 of the 154 patients with sepsis (68.2%). Of these, 99.0% (104/105) were infected with HIV-1. HIV was detected in 105 of the 154 patients with sepsis (68.2%). the median age is 43 (37-49) $< 0,001$ ; Of these, 99.0% (104/105) were infected

with HIV-1. Women accounted for 59.0% (n = 62), with a female-to-male ratio of 1.44. The in-hospital mortality rate among HIV-positive patients (20.0%) was not different from that among HIV-negative patients (20.4%; p = 1.0). The median length of hospital stay is 20 (18-23) days (p = 0.060). The other characteristics are shown in Table 1.

**Table 1:** General Characteristics of the cohort.

	N	(%)
Sex		
Women	62	59.0
Men	43	41.0
Education		
High school	74	70.4
University	22	21.0
Elementary school	5	4.8
Not school	4	3.8
Comorbidities		
Diabetes	21	20.0
HTA	22	21.0
Hepatitis B	3	2.9
Tuberculosis	9	8.6
Tobacco	11	10.5
alcohol	29	27.6
Clinical presentation		
Fever	35	71.4
Chills	28	57.1
Hypotension	40	81.6
qSOFA=3	32	65.3

### Antiretroviral coverage and virologic status

Only 31.4% of HIV patients were on antiretroviral therapy at admission (n = 33), leaving 68.6% (n = 72) untreated. The median viral load was 5.16 log copies/mL (IQR: 4.30-5.80), or 64,400 copies/mL in absolute terms. Nearly all patients had active viremia: 94.3% had a viral load of  $\geq 1,000$  copies/mL. Only 5.7% (n = 6) had a viral load  $< 1,000$  copies/mL, indicating viral suppression.

### Stade OMS et taux de CD4

The distribution by WHO stage was relatively even: stage 1 (26.7%; n = 28), stage 2 (26.7%; n = 28), stage 3 (22.9%; n = 24), and stage 4 (23.8%; n = 25). Advanced stages 3 and 4 together accounted for 46.7% of the cohort. The median CD4 count for the entire HIV cohort was 145 cells/mm<sup>3</sup> (IQR: 79-255), with a mean of 173  $\pm$  125 cells/mm<sup>3</sup>. 64.8% of patients had a CD4 count  $< 200$  cells/mm<sup>3</sup> and 12.4% had a CD4 count  $< 50$  cells/mm<sup>3</sup>. The negative correlation between CD4 count and WHO stage was strong and highly significant (r = -0.447; p < 0.0001): the median CD4 count decreased from 218 cells/mm<sup>3</sup> in stage 1 to 76 cells/mm<sup>3</sup> in stage 4. Conversely, viral load increased with disease stage (log 4.74 in stage 1 versus 5.70 in stage 4). Table 1 presents detailed immunovirological parameters by WHO stage.

**Table 2:** Immunovirological parameters by WHO stage (n = 105).

Setting	Stage 1 (n=28)	Stage 2 (n=28)	Stage 3 (n=24)	Stage 4 (n=25)	P
CD4 médian (cell/mm <sup>3</sup> )	218	210	122	76	<0,001
CD4 < 200 (%)	32 %	32 %	83 %	96 %	<0,001
CV log médiane	4,74	4,90	5,38	5,70	<0,05
Opportunist infections (%)	7 %	54 %	92 %	84 %	<0,001
Mortality	21,4 %	25,0 %	12,5 %	20,0 %	NS

NS: not significant

### Opportunistic infections and intercurrent illnesses

In total, 60 of 105 patients (57.1%) had at least one opportunistic infection. Tuberculosis was the most common infection (23.8%; n = 25), with 16 patients testing positive on the Xpert MTB/RIF.

These were followed by toxoplasmosis (8.6%; n = 9), candidiasis (6.7%; n = 7), coccidiosis (5.7%; n = 6), prurigo (3.8%), pneumocystosis (1.9%; n = 2), and herpes (1.0%). The increase in opportunistic infections according to WHO stage was very marked: from 7% in stage 1 to 92% in stage 3. Coccidiosis and pneumocystosis were concentrated among patients with very low CD4 counts ( $< 50$  cells/mm<sup>3</sup>), consistent with the classic patterns of WHO-defined opportunistic infections.

### Circumstances for HIV testing

Screening was primarily conducted in response to symptomatic clinical presentations. Weight loss was the most common presenting symptom (17.1%; n = 18), followed by cough with fever (10.5%; n = 11), chronic diarrhea (5.7%; n = 6), headache with fever (5.7%), dysphagia (4.8%), and acute diarrhea (3.8%). Only 12.4% of patients (n = 13) had undergone voluntary screening. This pattern of late screening, characterized by advanced clinical presentations, is consistent with the severe immunosuppression observed and the high prevalence of advanced stages (46.7% in stages 3-4).

### CD4 count and microbiological profile

The CD4 quartile analysis revealed an inverse relationship between CD4 count and opportunistic infections (85% in Q1 versus 23% in Q4) and a direct relationship between CD4 count and advanced WHO stage (81% of stages 3-4 in Q1 versus 19% in Q4). In contrast, no mortality gradient was observed across the quartiles (18.5%, 17.9%, 29.2%, and 15.4% in Q1-Q4, respectively), with a paradoxical peak in mortality in Q3 attributed to the high prevalence of *Klebsiella pneumoniae* in this subgroup (6 isolates, case fatality rate of 52.6%). Furthermore, the antibiotic resistance profile was independent of CD4 count (all p > 0.14), suggesting community-wide spread of MRBs unrelated to individual immune status. Table 3 summarizes these results by CD4 quartile.

**Table 3:** Clinical, microbiological, and prognostic characteristics by CD4 quartile.

Setting	Q1 5-79 (n=27)	Q2 80-145 (n=28)	Q3 150-255 (n=24)	Q4 261- 566 (n=26)	p
Mortality	18,5 %	17,9 %	29,2 %	15,4 %	NS
Bacteremia	55,6 %	46,4 %	66,7 %	61,5 %	NS
IO présents	85 %	82 %	33 %	23 %	<0,001
Stage OMS 3/4	81 %	57 %	25 %	19 %	<0,001
Dominant germ	E. coli	E. coli	K. pneumoniae	Sterile	—
C3G Resistance	66,7 %	76,9 %	87,5 %	68,8 %	NS
CV log médian	5,64	5,38	4,79	5,02	NS

NS: not significant

## Discussion

The median CD4 count of 145 cells/mm<sup>3</sup> and the proportion of 64.8% of patients with a CD4 count < 200 cells/mm<sup>3</sup> indicate very severe immunosuppression in this cohort. These values are similar to those reported in Nigerian and Tanzanian cohorts of HIV-associated sepsis, where median CD4 counts range from 100 to 200 cells/mm<sup>3</sup> [8,9]. Immunosuppression is a direct consequence of insufficient ARV coverage (31.4%), even though coverage in Gabon stands at 87%, which falls short of the 95% targets (95-95-95) recommended by UNAIDS [1]. This situation is not unique to our center: systematic reviews show that actual ART coverage in African hospital cohorts remains between 20% and 50% in many countries [10].

The median viral load of 5.16 log copies/mL reflects massive, uncontrolled viral replication in 94.3% of the cohort. This high viral load sustains chronic immune activation, impairs the response to invasive bacteria, and promotes organ dysfunction in the context of sepsis [11,12].

The strong correlation between CD4 count and the prevalence of opportunistic infections (r = -0.447, with a gradient ranging from 7% in stage 1 to 92% in stage 3) confirms the validity of CD4 count as a clinical marker of the risk of opportunistic infections. This result is fully consistent with international data [13,14]. Tuberculosis, which is present at all WHO stages, illustrates its cross-cutting nature in relation to HIV in sub-Saharan Africa, where it is the leading cause of HIV-related mortality [15]. The prevalence of coccidiosis and pneumocystosis in patients with CD4 counts < 50 cells/mm<sup>3</sup> meets the criteria for defining stage 4 opportunistic infections.

Only 12.4% of patients had undergone voluntary testing. Nearly all HIV diagnoses were based on symptomatic clinical presentations (weight loss, cough, diarrhea), reflecting insufficient access to routine testing. This delay in diagnosis is directly responsible for the progression to higher WHO stages: when HIV is diagnosed due to a symptom, it is often already at an advanced stage [16,17]. Innovative self-testing and home-based screening strategies are not yet available in our country to reduce this delay.

The lack of association between CD4, viral load and hospital mortality is the most original result of this work. This is explained by the fact that the immediate prognosis of sepsis is determined more by the virulence of the bacterial pathogen than by the chronic background of immunosuppression. The peak in Q3 mortality of CD4 (29.2%), linked to the concentration of *K. pneumoniae* (lethality 52.6%) in this subgroup, is the most striking illustration. This prioritization has direct implications: when faced with an HIV patient in sepsis, the absolute priority is appropriate empirical antibiotic therapy covering local MDR bacteria rather than prognostic stratification based on CD4.

This study does have some limitations. Its retrospective and single-center nature prevents the generalization of its results. Furthermore, there is a lack of previous data on the immunovirological monitoring of patients.

However, this study documents a severe immunovirological profile in HIV patients hospitalized for sepsis: profound immunosuppression (median CD4 count 145 cells/mm<sup>3</sup>), uncontrolled viremia (median viral load 5.16 log), insufficient ART coverage (31.4%), and late diagnosis, predominantly symptomatic. These data demonstrate a systemic breakdown in the HIV care pathway, from testing to treatment initiation and virological monitoring.

## Conclusion

CD4 count is a powerful marker of the risk of opportunistic infections, but it does not predict immediate sepsis mortality. Acute prognosis is more determined by microbial virulence, particularly *K. pneumoniae*, and resistance to third-generation cephalosporins. These findings highlight two simultaneous priorities: improving antiretroviral (ARV) coverage and early screening to prevent opportunistic infections that lead to sepsis, and revising empirical antibiotic therapy protocols to account for local resistance profiles to reduce acute mortality.

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