BMC Infectious Diseases

RESEARCH Open Access

Descriptive epidemiology of opportunistic infections among patients with advanced HIV disease in Kinshasa, Democratic Republic of Congo

Lucie Matsuela Bakana[1,2], Denis Mpika Mpika[2], Doudou Malekita Yobi[2], Pius Zakayi Kabututu[2], Patrick Tembeni Mwasomi[3], Pulcherie Ditondo[3], Marcel Mbula Mambimbi[4], Aimé Nkoso Mboyo[5], Tony Kalwangila Sequeira[5], Katrien Lagrou[6,7], Georges Lelo Mvumbi[2] and Bive Bive Zono[2*]

Abstract

Background Although people living with HIV (PLHIV) increasingly have access to antiretroviral therapy (ART) worldwide, the recurrence of advanced HIV disease (AHD) remains a major concern, exposing them to an enhanced risk of opportunistic infections (OIs) and subsequent death. We aimed here to describe the epidemiology of OIs among patients with AHD in Kinshasa (Democratic Republic of Congo, DRC) to inform future actions against AHD-related deaths.

Methods A retrospective cohort study was conducted among consecutive AHD patients admitted to Biyela Hospital Center in Kinshasa (DRC)—a peripheral clinic supported by Médecins Sans Frontières (MSF)-Belgium, between June 2021 and December 2023. The diagnosis of OIs was mainly based on MSF's advanced HIV management guidelines, establishing the diagnosis of tuberculosis using Determine TB-LAM Ag test and/or Xpert MTB/RIF, cryptococcal meningitis using the CrAg LFA antigen test, and malaria and syphilis using the corresponding Rapid diagnostic tests. For other OIs such as cerebral toxoplasmosis, oropharyngeal candidiasis, *Pneumocystis jirovecii* pneumonia, and nonspecific bacterial infections, diagnosis was essentially based on the clinician's clinical presumption, due to resource limitations. Descriptive statistics were performed using SPSS version 27.00.

Results Among the 130 included AHD patients (58.8% female, mean age 42 ± 16 years), 59.2% presented with multiple OIs. The most prevalent OIs were meningeal tuberculosis (61.5%), cerebral toxoplasmosis (51.5%), nonspecific bacterial pneumonia (33.1%), pulmonary tuberculosis (32.2%), cryptococcal meningitis (20.0%), nonspecific bacterial meningitis (18.5%), oropharyngeal candidiasis (17.7%), and cerebral malaria (10.8%). The clinical presentation of meningeal tuberculosis, cerebral toxoplasmosis, nonspecific bacterial pneumonia, nonspecific bacterial meningitis, and pulmonary tuberculosis was mainly characterized by fever (75%, 72.7%, 79.1%, 75%, 67.5%, respectively); cryptococcal meningitis by incoherent speech (77.7%); and oropharyngeal candidiasis by weight loss (68.2%).

*Correspondence:
Bive Bive Zono
bive.zono@unikin.ac.cd

Full list of author information is available at the end of the article

Conclusions Patients with AHD in Kinshasa (DRC) frequently experience multiple OIs. While the majority of these OIs are commonly recognized in the end-stage of HIV infection (tuberculosis, cerebral toxoplasmosis, cryptococcal meningitis, nonspecific bacterial infections, oropharyngeal candidiasis), cerebral malaria is another condition that should be considered in the DRC context.

Keywords Advanced HIV disease, Tuberculosis, Cryptococcosis, Toxoplasmosis, DRC

Background

Despite the increased accessibility and democratization of antiretroviral therapy (ART), with global treatment coverage reaching approximately 77% among people living with HIV (PLHIV) who are aware of their status, advanced HIV disease (AHD) remains a significant public health concern. This applies both to newly diagnosed patients and to those who have already undergone ART, particularly those with discontinuous treatment [1, 2].

While more than one-third of newly diagnosed PLHIV who are likely to start ART are already in the AHD stage [3], the proportion of patients presenting with AHD despite being on ART in some sub-Saharan African countries reaches up to two-thirds [4, 5]. In this context, the enhanced mortality commonly reported among AHD patients compared to non-AHD patients is usually a consequence of the prevalent fatal opportunistic infections (OIs) that occur at the end-stage of HIV infection, alongside many other causes [6].

With an estimated overall prevalence of 0.7% in the general population aged 15 to 49, the Democratic Republic of Congo (DRC) has nearly 610,000 PLHIV, 23% of whom are unaware of their HIV status. Of those who test positive, nearly one-third (29%) unfortunately do not have access to ART [7]. Assessing HIV disease in patients admitted to initiate ART in six health zones (of 35) in Kinshasa, a study found that 32% of patients already had AHD, including adults, children, and adolescents [8]. At a Médecins Sans Frontières (MSF) clinic in Kinshasa specializing in AHD care, 58% of patients receiving outpatient ART initiation care had a CD4 count of ≤200/µl. Furthermore, upon admission to hospital, around 70% of patients were in the end-stage of HIV disease (CD4≤200 cells/µl) [9]. Opportunistic infections developing particularly in this highly vulnerable population are mainly identified as one of the main causes of death among PLHIV [10, 11]. Despite these alarming findings, few urgent measures have been implemented to address the recurrence of this public health problem and its devastating consequences for affected PLHIV. In Kinshasa, for instance, which has around 20 million inhabitants and where 0.4% of people aged 15–49 would be infected with HIV [12], fewer than five healthcare facilities provide the full package of services for AHD care (Advanced HIV Activity Report, National HIV/AIDS Control Program – DRC, 2024).

Regarding OIs, which also must be targeted in order to end AHD-related deaths, they are often described in isolation without integrating the fact that a patient could develop more than one OI concurrently, thus further increasing the risk of his death [13–16]. Furthermore, these OIs are often documented without focusing exclusively on the population affected by AHD, which is most susceptible to developing these infections, making it difficult to accurately assess the epidemiological burden in this specific HIV-infected population [9, 17]. Not only are data updates necessary, but an integrated description of consecutive cases highlighting the implications of possible multiple OIs in the same patient is also important.

The present study aimed to describe the clinical epidemiology of OIs in consecutive AHD patients hospitalized at a MSF-supported clinic in Kinshasa (DRC), taking also co-OIs into account.

Methods

Study design

A retrospective cohort analysis was conducted based on the medical records of patients consecutively hospitalized for OIs at the Saint-Joseph BIYELA Hospital Center from June 2021 to December 2023.

Patients

Only PLHIV hospitalized during the study period for any HIV-related medical condition with available medical records were considered in the study. Individuals for whom study-related data were missing were excluded.

Study site

Saint-Joseph BIYELA Hospital Center is a medical institution run by the Catholic Sisters of Saint-Joseph, located in the BIYELA health zone, in a remote suburb of Kinshasa (DRC). The Center has 72 hospital beds organized into four main basic clinical services (Internal Medicine, Pediatrics, Surgery, and Gynecology-Obstetrics) where PLHIV receive care tailored to their health condition, thus avoiding any discrimination or marginalization. Since 2020, the Center has benefiting from the holistic support from MSF-Belgium for HIV outpatients' follow-up and AHD-related care, including training and mentoring for healthcare staff, provision of basic laboratory equipment and logistics, supply of laboratory reagents and essential medicines, contribution to operating costs, and even psychological support for PLHIV.

Diagnostic criteria

In addition to the primary study parameter (OIs developed by the patients), demographic, clinical and biological parameters were retrieved from the patients' medical records. Clinical syndromes observed at admission were defined based on the MSF HIV/TB treatment guidelines for hospitals, taking into account the predominant clinical signs of severity [18]. All clinical signs were assessed by the MSF doctor who admitted the patient.

Based on WHO definitions, AHD patients were defined as having a CD4 count of ≤ 200 cells/µl, and/or having experienced at least one stage 3 or 4 clinical event at the time of admission, as well as all children under 5 years of age with HIV [19]. In the study clinic, OIs are managed according to protocols based on WHO recommendations, which are sometimes adapted to local conditions [20]. The Alere PIMA CD4 analyzer (Alere Inc., Waltham, MA, USA) was used for quantitative CD4 counting, and the VISITEC test (AccuBio Ltd, Scotland, UK) was used for qualitative CD4 counting when the former was out of stock. HIV viral load (VL) was measured using the Abbott m2000 system, as previously described [21, 22]. Basic hematological analyses were performed on the Sysmex XP-300 automated analyzer (Wakinohama-Kaigandori, Kobe, Japan).

In accordance with MSF's advanced HIV care guidelines and considering each patient's clinical presentation [18], cryptococcal infections were diagnosed using the CrAg LFA IMMY antigen test (Immuno-Mycologics, Norman, OK, USA) in the blood and/or cerebrospinal fluid (CSF) depending on the clinical suspicion; *Mycobacterium tuberculosis* infections using the Determine TB-LAM Ag test in urine (Alere Inc., Waltham, MA, USA), or the Xpert MTB/RIF assay (Cepheid Inc., Sunnyvale, CA, USA) in other body fluids (sputum, CSF…); malaria using malaria rapid diagnostic tests (RDTs) and/or thick smears; and syphilis using syphilis RDTs, according to the respective manufacturers' instructions. Cerebral toxoplasmosis, oropharyngeal candidiasis, *Pneumocystis jirovecii* pneumonia, peripheral neuropathies, and immune reconstitution inflammatory syndrome (IRIS) were presumptive diagnoses based on the clinical presentation of the patients, in accordance with MSF's clinical decision-making algorithm [18]. Bacterial infections of any organ were mainly diagnosed on the basis of clinical suspicion and routine infectious/inflammatory biological tests [white blood cell (WBC) count, leukocyte formula, blood sedimentation rate, C-reactive protein, cerebrospinal fluid cytochemistry]. For lung involvement, in addition to the clinical presentation of patients on admission and the biological tests performed, chest X-rays were also used to support the diagnosis. MSF management guidelines were strictly applied with regard to the treatment of various OIs in AHD [20].

Statistics

Statistical analyses were performed using the Windows version 27.0 of the SPSS software (IBM, Chicago, USA). Continuous quantitative variables were summarized as the mean ± standard deviation (SD) or the median [and interquartile range (IQR)] as appropriate. Proportions and their respective 95% confidence intervals (CI) were calculated for categorical data. Qualitative CD4 counts of < 200 or ≥ 200 cells/µl were rounded to the median of the quantitative values for each range to standardize the data for quantitative statistics. Similarly, HIV viral load results for which the target was not detectable (< 40 copies/µl) were rounded up to 40 copies/µl to facilitate quantitative analysis. Missing data were considered to be completely random, and analysis was performed on the available data after excluding variables with substantial missing data.

Results

Demographic, clinical, and biological characteristics of the patients

A total of 137 patient medical records were analyzed, of which seven were excluded due to incomplete data. Among the 130 PLHIV included, 8.5% (11/130) were referred from the MSF-Kinshasa referral clinic for continuity of care previously initiated, and 91.5% (119/130) were initial admissions to the BIYELA Hospital Center. The majority of patients were female (58.8%), with an average age of 42.4 ± 13.8 years, and mainly coming from the Tshangu district (one of the four districts of Kinshasa) where the study site is located (87.7%).

At admission, the predominant clinical syndromes were neurological syndrome associated with respiratory syndrome (46.9%, 61/130), neurological syndrome alone (32.3%, 42/130), and digestive syndrome alone (13.1%, 17/130). The most prevalent clinical manifestations upon admission were fever (66.9%), unquantified weight loss (62.3%), cough (50.8%), asthenia (44.6%), headache (27.7%), and altered consciousness (26.2%). The physical examination was essentially marked by meningeal irritation signs in 14.8% of patients, oral lesions suggestive of oral candidiasis (17.7%), and Kaposi's sarcoma (3.1%). Overall, the vital signs of the patients were within physiological limits.

While all patients included were clinically classified as either stage 3 or 4 of HIV disease, nearly half of them were newly diagnosed HIV infection and were not yet receiving ART (45.5%, 55/121). Whilst most patients (90.6%) receiving ART were on the first-line triple therapy recommended in the DRC (TDF+3TC + DTG), 36.4% had interrupted ART at least once in the past for undeclared reasons. In the present cohort, 30.8% had a history of tuberculosis, and 90.6% received prophylactic doses of

Table 1 Demographic, clinical and biological characteristics

Characteristics*	Overall data (%)**	95% CI
Demographic characteristics		
Female sex (*n* = 114)	67 (58.8)	49.1–67.5
Mean age ± SD (years) (*n* = 128)	42.41 ± 13.8	-
District of origin (*n* = 114)		
Tshangu	100 (87.7)	81.6–93.0
Funa	10 (8.8)	3.5–14.0
Mont Amba	3 (2.3)	0.0–6.1
Lukunga	1 (0.9)	0.0–2.6
Clinical characteristics upon admission		
Predominant clinical syndrome (n = 130)		
Neurological syndrome associated with respiratory syndrome	61 (46.9)	38.5–55.4
Neurological syndrome alone	42 (32.3)	24.6–40.8
Digestive syndrome alone	17 (13.1)	7.7–19.2
Respiratory syndrome alone	16 (12.3)	6.9–18.5
Dermatological syndrome alone	4 (3.1)	0.8–6.2
Main symptoms/signs (n = 130)		
Fever	87 (66.9)	58.5–75.4
Weight loss	81 (62.3)	54.6–70.0
Cough	66 (50.8)	42.3–59.2
Asthenia	58 (44.6)	36.2–53,8
Headaches	36 (27.7)	20.0–35.4
Impaired consciousness	34 (26.2)	18.5–33.8
Dizziness	20 (15.4)	10.0–22.3
Incoherent speech	17 (13.1)	6.9–19.2
Dysphagia	13 (10.0)	5.4–16.1
Behavioral disorders	12 (9.2)	4.6–14.6
Logorrhea	12 (9.2)	4.6–14.6
Vital parameters		
Mean heart rate ± SD (bpm) (*n* = 124)	101.7 ± 16.8	-
Mean temperature ± SD (°C) (*n* = 125)	36.8 ± 0.9	-
Mean respiratory rate ± SD (cpm) (*n* = 126)	22.5 ± 5.3	-
Mean O_2 saturation ± SD (mmHg) (*n* = 116)	97.9 ± 3.8	-
Clinical examination		
Meningeal irritation (*n* = 115)	17 (14.8)	8.7–20.9
Oral examination (*n* = 130)		
No particular features	101 (77.7)	70.0–84.6
Candidal lesions	23 (17.7)	10.8–24.6
Kaposi's sarcoma lesions	4 (3.1)	0.8–6.2
Cold sores lesions	2 (1.5)	0.0-4.6
Biological characteristics upon admission		
Mean Hb ± SD (mg/dl) (*n* = 110)	9.3 ± 2.46	-
WBC (cells/µl) [median (IQR)] (*n* = 42)	4650 (3450–7000)	-
Neutrophilic leukocyte formula (*n* = 31)	27 (87.1)	(74.2–96.8)
Blood sugar (md/dl) [median (IQR)] (*n* = 108)	104 (87–127)	-
Creatinine (µmol/l) [median (IQR)] (*n* = 110)	96.7 (70.7–152)	-
Alanine transaminase [median (IQR)] (IU/l) (*n* = 94)	27.6 (18.3–47.0)	-

*according to available data; **Column per cent calculated for each group

Table 2 Clinical and biological characteristics related to HIV disease

HIV characteristics*	Overall data (%)**	95% CI
HIV clinical stage (*n* = 124)		
Stage 3	21 (16.9)	10.5–23.4
Stage 4	103 (83.1)	76.6–89.5
ART statute upon admission (*n* = 121)		
Naive	55 (45.5)	36.4–55.4
Non-naive	66 (54.5)	44.6–63.6
ART duration (year) (*n* = 64) ***		
< 1	21 (32.8)	21.9–43.8
2–5	18 (28.1)	17.2–40.6
> 5	25 (39.1)	28.1–51.6
Current ART (*n* = 64)***		
TDF/3TC/DTG	58 (90.6)	82.8–96.9
ABC/3TC/DTG	1 (1.6)	0.0-4.7
AZT/3TC/DTG	2 (3.1)	0.0-7.8
ART interrupted	1 (1.6)	0.0-4.7
ART not indicated	2 (3.1)	0.0-7.8
Cotrimoxazole prophylaxis (*n* = 66)	62 (93.9)	87.9–98.5
Previous ART interruption (*n* = 66)	24 (36.4)	24.2–48.5
CD4 (cells/µl) [median (IQR)] (*n* = 128)	199 (62.75–202.75)	-
HIV viral load (copies/µl) [median (IQR)] (*n* = 47)	7553 (40–305690)	-

TDF=Tenofovir disoproxil fumarate; 3TC=Lamivudine; DTG=Dolutegravir; ABC=Abacavir; AZT=Zidovudine

*according to available data; **Column per cent calculated for each group; ***Two patients were on complete ART interruption on admission

cotrimoxazole against susceptible OIs (such as toxoplasmosis, isosporiasis, malaria).

The median CD4 T-cell count was 199 (63–203) cells/µl, and the median viral load was 7553 (40-305690) copies/µl at the time of hospitalization. The demographic, clinical, and biological characteristics of all included PLHIV are detailed in Table 1; and the clinical and biological characteristics related to HIV infection of patients are shown in Table 2.

Prevalence of opportunistic infections in hospitalized patients with AHD

As shown in Table 3, the main OIs encountered in the study population were meningeal tuberculosis (61.5%; 80/130), cerebral toxoplasmosis (51.5%; 67/130), bacterial pneumonia (33.1%; 43/130), pulmonary tuberculosis (32.2%; 42/130), cryptococcal meningitis (20.0%; 26/130), bacterial meningitis (18.5%; 24/130), oropharyngeal candidiasis (17.7%; 23/130), and cerebral malaria (10.8%; 14/130). Among these infections, only meningeal tuberculosis, pulmonary tuberculosis, cryptococcal meningitis, and cerebral malaria were confirmed/probable diagnoses; the others were diagnosed primarily on the basis of clinical presentation, general laboratory tests, and/or therapeutic response after therapeutic trial.

Table 3 Opportunistic infections in patients with advanced HIV disease

Opportunistic infections	Overall data (%) n=130	95% CI
Meningeal tuberculosis	80 (61.5)	52.3 – 70.0
Cerebral toxoplasmosis	67 (51.5)	43.1 – 60.8
Nonspecific bacterial pneumonia	43 (33.1)	25.4 – 40.8
Pulmonary tuberculosis	42 (32.3)	23.8 – 40.0
Cryptococcal meningitis	26 (20.0)	13.1 – 26.9
Nonspecific bacterial meningitis	24 (18.5)	12.3 – 25.4
Oropharyngeal candidiasis	23 (17.7)	11.5 – 24.6
Cerebral malaria	14 (10.8)	5.4 – 16.2
Isolated bloodstream cryptococcosis	8 (6.2)	2.3 – 10.8
Kidney failure	8 (6.2)	2.3 – 10.0)
Pneumocystis jirovecii pneumonia	5 (3.8)	0.8 – 7.7
Kaposi's sarcoma	2 (1.5)	0.0-3.8
Stroke	2 (1.5)	0.0-3.8
IRIS-TB*	2 (1.5)	0.0-3.8

*immune reconstitution inflammatory syndrome-TB

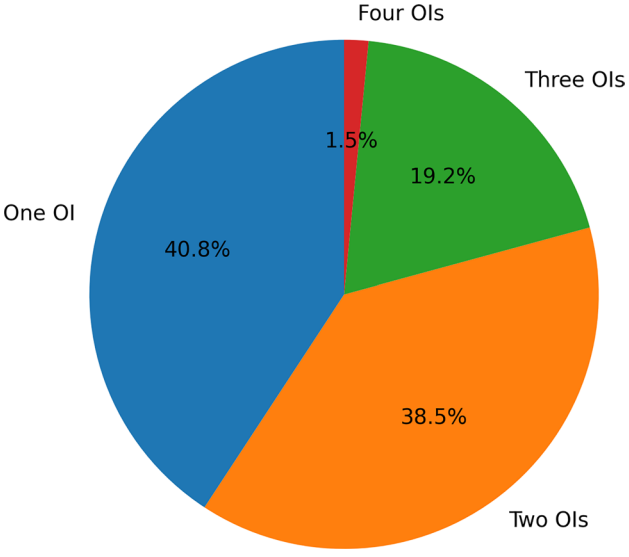

Fig. 1 Distribution of AHD patients according to the number of opportunistic infections (OIs) presented during hospitalization

Considering the possibility of multiple OIs in the same person, more than half of the patients were infected with more than one OI (59.2%, 77/130). As shown in Fig. 1, nearly one in five patients (19.3%) was simultaneously infected with three OIs. Particularly, more than a quarter of patients (27.8%) were found to be infected with both cerebral toxoplasmosis and meningeal tuberculosis, while nearly one-tenth (8%) were infected with three concurrent OIs: cerebral toxoplasmosis, bacterial meningitis, and meningeal tuberculosis. Furthermore, 6% of patients were found to be infected with cryptococcal meningitis, cerebral toxoplasmosis, and meningeal tuberculosis.

Regarding the clinical presentation of patients in relation to diagnosed OIs, meningeal tuberculosis (75%), cerebral toxoplasmosis (72.7%), nonspecific bacterial pneumonia (79.1%), nonspecific bacterial meningitis (75%), and pulmonary tuberculosis (67.5%) were mainly characterized by fever; cryptococcal meningitis by incoherent speech (77.7%); and oropharyngeal candidiasis by weight loss (68.2%). The distribution of opportunistic infections according to clinical parameters is detailed in Table 4.

Discussion

We described here the clinical and biological epidemiology of OIs in 130 patients with AHD who have consecutively been hospitalized at a clinic supported by MSF in Kinshasa (DRC).

While the demographic profile of included patients was comparable to that of PLHIV in the DRC [7], nearly half of the patients (46%) with AHD were newly diagnosed and therefore ART-naïve. This observation is consistent with global and local data from the DRC on the alarming proportion of patients diagnosed at the terminal stage of HIV disease, ranging from 31.5% to 49.6% [3, 8, 19]. This highlights concerns about barriers to early diagnosis of HIV infection, at a time when the package of care for uncomplicated HIV appears to be freely accessible and available in hospitals within the DRC health system. Referring to the African context, age, male gender, fear of stigmatization by others, poor emotional health, significant distance between home and hospital, competing needs to healthcare, barriers to access to care in general, and working far from home, may partially explain the late presentation of these patients to the hospital [23, 24]. Although numerous efforts are being implemented by the national AIDS control program in the DRC to improve screening of populations, particularly through the community relay sector, there is a need for reinforcement in order to reach more people and improve results at the ground level.

In this study, OIs were dominated by tuberculosis (meningeal and pulmonary), cerebral toxoplasmosis, nonspecific bacterial infections (meningeal and pulmonary), meningeal cryptococcosis, oropharyngeal candidiasis, and cerebral malaria. These results closely corroborate the list of recurrent and fatal opportunistic infections in patients with AHD published by the WHO, the control of which is recognized by this global institution as the cornerstone for ending HIV-related deaths [19]. In addition to the OIs that are well-documented in this population, cerebral malaria is also emerging as a significant infection in the terminal stage of HIV disease, although it is not really considered an OI. Given its endemic status in the DRC, it is necessary to consider this parasitic infection in global measures to combat AHD-related deaths in this country [25].

Table 4 Opportunistic infections according to clinical parameters

Parameters	Opportunistic infections (*n* = 130)						
	MT [*n* (%)]	CT [*n* (%)]	NBP [*n* (%)]	PT [*n* (%)]	CM [*n* (%)]	NBM [*n* (%)]	OC [*n* (%)]
Behavioral disorders	9 (11.3)	10 (15.1)	6 (13.9)	3 (7.5)	1 (3.8)	1 (4.2)	2 (9.1)
Asthenia	28 (35.0)	21 (31.8)	23 (53.5)	26 (65.0)	9 (34.6)	9 (37.5)	12 (54.5)
Impaired consciousness	27 (33.8)	25 (37.9)	10 (23.3)	7 (17.5)	6 (23.1)	7 (29.2)	1 (4.5)
Fever	60 (75.0)	48 (72.7)	34 (79.1)	27 (67.5)	16 (61.5)	18 (75.0)	14 (63.6)
Cough	46 (57.5)	35 (53.0)	28 (65.1)	21 (52.5)	8 (30.8)	11 (45.8)	13 (59.1)
Headaches	28 (35.0)	19 (28.8)	13 (30.2)	6 (15.0)	10 (38.5)	8 (33.3)	3 (13.6)
Weight loss	53 (66.3)	44 (66.7)	32 (74.4)	23 (57.5)	15 (57.7)	11 (45.8)	15 (68.2)
Night sweats	8 (10.0)	6 (9.1)	4 (9.3)	2 (5.0)	1 (3.8)	3 (12.5)	2 (9.1)
Convulsions	6 (7.5)	5 (7.5)	2 (4.7)	0 (0.0)	0 (0.0)	2 (8.3)	1 (4.5)
Dysphagia	6 (7.5)	4 (6.1)	5 (11.6)	7 (17.5)	0 (0.0)	1 (4.2)	12 (54.5)
Dizziness	13 (16.3)	7 (10.6)	8 (18.6)	6 (15.0)	3 (11.5)	6 (25.0)	4 (18.2)
Vomiting	5 (6.3)	2 (3.0)	2 (4.7)	4 (10.0)	4 (15.4)	3 (12.5)	2 (9.1)
Anorexia	7 (8.8)	5 (7.5)	4 (9.3)	3 (7.5)	3 (11.5)	2 (8.3)	4 (18.2)
Logorrhea	7 (8.8)	8 (12.1)	3 (6.9)	4 (10.0)	2 (7.7)	5 (20.8)	2 (9.1)
Incoherent speech	14 (17.5)	14 (21.2)	11 (25.6)	3 (7.5)	2 (77.7)	2 (8.3)	1 (4.5)
Motor impotence	7 (8.8)	6 (9.1)	4 (9.3)	3 (7.5)	0 (0.0)	2 (8.3)	2 (9.1)

MT: meningeal tuberculosis; CT: cerebral toxoplasmosis; NBP: nonspecific bacterial pneumonia; PT: pulmonary tuberculosis; CM: cryptococcal meningitis; NBM: nonspecific bacterial meningitis; OC: Oral-esophageal candidiasis

It is noteworthy that more than half of the patients in the study were infected with more than one pathogen, which has the potential to further increase the risk of death and disability after discharge from hospital, as has been previously demonstrated [26]. The high proportion of patients with multiple OIs highlights the diagnostic and therapeutic challenges faced by clinicians managing AHD in resource-limited hospital settings. Improvements in the care of AHD patients must therefore take into account WHO guidelines, reinforced by responses to the specific characteristics of the disease in each region, in view of the particulars outlined here.

With regard to the clinical presentation of patients on admission, tuberculosis (meningeal and pulmonary), cerebral toxoplasmosis, and nonspecific bacterial infections (meningeal and pulmonary) were mainly manifested by fever; cryptococcal meningitis by incoherent speech; and oropharyngeal candidiasis by weight loss. Although this is consistent with the known definition of these infections and their clinical complications [27], in the context of multiple OIs in the same patient as described here, these clinical trends have very minimal diagnostic value.

In the context of resource-limited countries such as those in this study, the diagnosis of OIs was either confirmed/probable or possible depending on the availability of diagnostic confirmation tools. Nosological entities such as cerebral toxoplasmosis, oropharyngeal candidiasis, *Pneumocystis jirovecii* pneumonia, and nonspecific bacterial infections were mainly diagnosed based on the clinician's clinical presumption. This, combined with the above considerations, further compromises the strength of the diagnostic presumption of IOs, highlighting the urgent need to expand access to specific diagnostic tests to ensure better patient care.

Study limitations

As with any retrospective study conducted in a medical facility where patient records are not computerized, this study suffered from some data loss due to poor record-keeping and patient registry systems. Secondly, in the context of multiple opportunistic infections as reported in this study, the presumptive diagnosis has little value. Biological confirmation would add further value to the study.

Conclusions

Although more than half of patients with advanced HIV disease were affected by more than one opportunistic infection, the main infections diagnosed were tuberculosis (meningeal and pulmonary), presumptive cerebral toxoplasmosis, presumptive bacterial infections (pulmonary and meningeal), meningeal cryptococcosis, presumptive oropharyngeal candidiasis, and cerebral malaria. In considering actions against advanced HIV disease-related deaths, cerebral malaria should also be considered alongside opportunistic infections in the DRC.

Abbreviations

3TC	Lamivudine
ABC	Abacavir
AHD	Advanced HIV Disease
AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral Treatments
AZT	Zidovudine

CD4	Cluster of Differentiation 4
CI	Confidence Intervals
CSF	CerebroSpinal Fluid
DRC	Democratic Republic of Congo
DTG	Dolutegravir
HIV	Human Immunodeficiency Virus
IQR	Interquartile Range
IRIS	Immune Reconstitution Inflammatory Syndrome
MSF	Médecins Sans Frontières
OI	Opportunistic Infection
OR	Odds Ratio
PLHIV	People Living with HIV
RDT	Rapid Diagnostic Tests
SD	Standard Deviation
TDF	Tenofovir disoproxil fumarate
WBC	White Blood Cell
WHO	World Health Organization

Acknowledgements
We would like to express our sincere gratitude to the management team at the BIYELA Medical Center for granting us access to the (sensitive) medical records of HIV patients treated at this healthcare facility.

Author contributions
Conceptualization: BBZ, LMB and DMM; methodology: BBZ, DMY and PKZ; validation: PTM, PD, ANM and GLM; formal analysis: BBZ, LMB and DMM; investigation: LMB and DMM; resources: PTM, PD, ANM, TKS, LMB and DMM; data curation: PTM, PD, ANM and TKS; writing—original draft preparation: BBZ, PTM, KL and MMM; writing—review and editing: GLM, MMM, KL, PKZ; visualization: BBZ and DMY; supervision: KL, GLM, BBZ. All authors agreed to bear responsibility for all parts of this manuscript and approved the final version.

Funding
The authors received no specific funding for this work.

Data availability
All data analyzed and generated in this study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The Ethics Committee of the Public Health School of the Faculty of Medicine of the University of Kinshasa (DRC) approved this study, which is part of a series of studies on OIs in HIV patients in Kinshasa being conducted by our research team (approval number: *ESP/CE/183/2024*). As the study data were collected retrospectively long after the patients had been discharged from hospital, informed consent was not obtained from the participants. This was also deemed inappropriate by the ethics committee in view of the retrospective nature of the study (including all known local difficulties in tracing patients after discharge) and the fact that only anonymized/de-identified patient records were considered. Although this, authorization to access medical records and use the data for scientific publication purposes was obtained from the clinic's religious leaders and the MSF team (who also participated in the study). Ethical rules regarding patient privacy and anonymity were rigorously respected in accordance with the principles of Helsinki. The data collected for this study were completely depersonalized and used solely and exclusively for study purposes.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Oral and Maxillofacial Surgery, University Clinics of Kinshasa, Faculty of Dental Medicine, Kinshasa, Democratic Republic of Congo
[2]Service of Molecular Biology, Department of Basic Sciences, Faculty of Medicine, University of Kinshasa, Kinshasa, Democratic Republic of Congo
[3]Médecins Sans Frontières (-Belgium), Kinshasa, Democratic Republic of Congo
[4]Infectious Diseases Service, Department of Internal Medicine/Department of Tropical Medicine, University Clinics of Kinshasa, Kinshasa, Democratic Republic of Congo
[5]Programme National de Lutte contre le SIDA/IST, Kinshasa, Democratic Republic of Congo
[6]Department of Laboratory Medicine, National Reference Center for Mycosis, University Hospitals Leuven, Leuven, Belgium
[7]Department of Microbiology, Immunology and Transplantation, University Hospitals Leuven, KU Leuven, Leuven, Belgium

Received: 20 January 2026 / Accepted: 31 March 2026
Published online: 03 April 2026

References

1. ONUSIDA. Fiche d'information 2024: Statistiques mondiales sur le VIH. 2025 https://www.unaids.org/sites/default/files/2025-07/UNAIDS_FactSheet_fr.pdf.
2. Boyd AT, Oboho I, Paulin H, Ali H, Godfrey C, Date A, et al. Addressing advanced HIV disease and mortality in global HIV programming. AIDS Res Ther. 2020;17(1):1–7.
3. Ford N, Kassanjee R, Stelzle D, Jarvis JN, Sued O, Perrin G, et al. Global prevalence of advanced HIV disease in healthcare settings: a rapid review. J Int AIDS Soc. 2025;28(2):1–12.
4. Owachi D, Akatukunda P, Nanyanzi DS, Katwesigye R, Wanyina S, Muddu M, et al. Mortality and associated factors among people living with HIV admitted at a tertiary-care hospital in Uganda: a cross-sectional study. BMC Infect Dis. 2024;24(1):1–10.
5. Kitenge MK, Fatti G, Eshun-wilson I, Aluko O, Nyasulu P. Prevalence and trends of advanced HIV disease among antiretroviral therapy-naïve and antiretroviral therapy-experienced patients in South Africa between 2010–2021: a systematic review and meta-analysis. BMC Infect Dis. 2023;23(549):1–16. https://doi.org/10.1186/s12879-023-08521-4.
6. Manosuthi W, Chaovavanich A, Tansuphaswadikul S, Prasithsirikul W, Inthong Y, Chottanapund S, et al. Incidence and risk factors of major opportunistic infections after initiation of antiretroviral therapy among advanced HIV-infected patients in a resource-limited setting. J Infect. 2007;55(5):464–9.
7. UNAIDS info. Country factsheets Democratic Republic on Congo | 2024 HIV and AIDS Estimates. 2025.
8. Chabikuli ON, Ditekemena JD, Sigwadhi LN, Mulenga A, Mboyo A, Bidashimwa D, et al. Advanced HIV Disease at Antiretroviral Therapy Initiation and Treatment Outcomes Among Children and Adolescents Compared to Adults Living With HIV in Kinshasa, Democratic Republic of the Congo. J Int Assoc Provid AIDS Care. 2023;22:1–10.
9. Medecins Sans Frontières SA. Les négligés de l'infection au VIH Patients en stade VIH avancé: une prise en charge adaptée et gratuite est leur seule chance de survie. Ghizlaine. 2017. KInshasa https://samumsf.org/sites/default/files/2017-08/MSFKinshasaReportdigital_0.pdf.
10. Tepungipame AT, Tonen-wolyec S, Kalla GC, Longembe EB. Predictors of AIDS-related death among adult HIV-infected inpatients in Kisangani, the Democratic Republic of Congo. Pan Afr Med J. 2020;37(144):1–9.
11. Mulisya O, Sikakulya FK, Afodun AM, Mambo SB, Mulisya O. Rate of Art Adherence and Clinical Outcome Among HIV Patients with Opportunistic Infection in an Urban Hospital in Eastern DRC. Clin Res. 2024;5(1):1–9.
12. RDC-Institut National de la Statistique, Kinshasa E, de SP de ICF. Enquête Démographique et de Santé de République Démocratique du Congo 2023–2024: 2024 https://drc.unfpa.org/sites/default/files/pub-pdf/2025-02/RDC%2CEDS2023–2024.pdf.
13. Mahimba BN, Lowa PO, Aimée Mampasi Lulebo. Frequency and management of opportunistic infections in people living with advanced stage HIV on antiretroviral treatment in the city of Kinshasa, Democratic Republic of the Congo. Ann Africaines Médecine Artic Orig. 2025;18(3):6168–77.
14. Zono BB, Sacheli R, Situakibanza NH, Kabututu ZP, Ka A, Mbula MM, et al. Clinical epidemiology and high genetic diversity amongst Cryptococcus spp. isolates infecting people living with HIV in Kinshasa, Democratic Republic of Congo. PLoS ONE. 2022;17(5):1–15.
15. Zono B, Kamangu E, Situakibanza H, Amaela E, Bepouka B, Mbula M, et al. Epidemiological, clinical and biological profile of neuromeningeal

cryptococcosis among people living with HIV in Kinshasa, Democratic Republic of Congo. Pan Afr Med J. 2020;37(302):1–9.
16. Kivukuto Mutendela J, Mashupe SBMD, MK. HIV screening among patients followed for cryptococcal meningitis in developing countries: Data from Bukavu in the Democratic Republic of Congo. Afr J Microbiol Res. 2014;8(7):721–3.
17. Mbula M, Situakibanza H, Mananga L, Longokolo M, Mandina N, Mayasi N, et al. Profils clinique et biologique du VIH à Kinshasa Clinical and biological profile of people living with HIV / AIDS followed in the Infectious Diseases Service of the University Hospital of Kinshasa (Democratic Republic of the Congo) Arti. Rev MALI Infect Mirobiol. 2020;15:21–9.
18. Médecins Sans Frontières - Southern Africa Medical Unit (SAMU). Guide MSF VIH/TB Niveau Hôpital. Médecins Sans Front - South Afr Med Unit. 2021:1–42. https://www.msf.org.za/news-and-resources/msf-hivtb-guide-hospital-level.
19. Le T. World Health Organization Guidelines for managing advanced HIV disease and rapid initiation of antiretroviral therapy. https://doi.org/10.1080/01449298308914472.
20. Frontières MS. *Manuel clinique MSF VIH / TB pour les soins de santé primaires*. 2018 https://medicalguidelines.msf.org/sites/default/files/2023-06/MSF International Manuel clinique MSF VIH TB pour les soins de santé primaires Guideline v3 20210801 FR.pdf.
21. Alere TM. Pima ™ Analyser - Manuel d'utilisation. 2014.
22. Abbott Laboratories. Abbott RealTime HCV. 2011.
23. Ngongo NM, Nani-Tuma HS, Mambimbi MM, Mashi ML, Izizag BB, Ndolumingu FK, et al. Decrease in late presentation for HIV care in Kinshasa, DRC, 2006–2020. AIDS Res Ther. 2021;18(1):1–7.
24. Drain PK, Losina E, Parker G, Giddy J, Ross D, Katz JN, et al. Risk Factors for late-stage HIV disease presentation at initial HIV diagnosis in Durban, South Africa. PLoS ONE. 2013;8(1). https://doi.org/10.1371/journal.pone.0055305.
25. Bain LE, Dobermann D, Malaria. HIV and TB in the Democratic Republic of the Congo: Epidemiology, disease control challenges and interventions Question What is the evidence on epidemiology (including demographic and geographic inequalities) and disease control challenges of mal. 2022 https://doi.org/10.19088/K4D.2022.034
26. Meng S, Tang Q, Xie Z, Wu N, Qin Y, Chen R, et al. Spectrum and mortality of opportunistic infections among HIV / AIDS patients in southwestern China. Eur J Clin Microbiol Infect Dis. 2023;42:113–20.
27. Ramesh K, Gandhi S, Rao V. Clinical profile of human immunodeficiency virus patients with opportunistic infections: A descriptive case series study. Int J Appl Basic Med Res. 2015;5(2):119–23.

Publisher's note