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Clinical and virological outcomes in people with advanced HIV disease initiating a locally manufactured integrase inhibitor–based regimen: A prospective cohort study

Aya M. Al-sharif^{1,2}✉, Rasha Ahmed Abdalaziz¹, Ahmed Cordie^{1,2}, Zeinab Abdellatif⁴, Hend Hamed Tamim³, Mohamed B. Hashem¹, Rahma Mohamed^{1,2}, Ahmed M. Kamel⁴, Lamiaa Al Sehemy^{1,2}¹Hepatogastroenterology and Endemic Medicine Department–Faculty of Medicine, Cairo University, Egypt²Kasr Al-Aini HIV and Viral Hepatitis Fighting Group, Cairo University Hospitals, Cairo, Egypt³Clinical and Chemical Pathology Department, Faculty of Medicine, Cairo University, Egypt⁴Clinical Pharmacy Department, Faculty of Pharmacy, Cairo University, Egypt

ABSTRACT

Objective: To assess clinical, immunological, and virological responses to locally manufactured integrase-based antiretroviral therapy (ART) over nine months in treatment-naïve advanced HIV disease individuals and to identify early mortality prognostic factors.

Methods: This prospective cohort study conducted at a HIV Clinic (March 2023–August 2024) enrolled treatment-naïve individuals with advanced HIV disease. Key variables of interest included CD4 T-cell count (flow cytometry), HIV-1 RNA viral load (real-time PCR), nutritional and anthropometric indices (body mass index, mid-upper arm circumference, prognostic nutritional index) and sarcopenia (EWGSOP criteria), were assessed at baseline and at 3, 6, and 9 months. Comprehensive assessments also included clinical evaluation, standard laboratory parameters, and imaging studies.

Results: The cohort included 50 treatment-naïve individuals with advanced HIV disease. They had a mean age of 37.6 years (76% male), with a median baseline CD4 count 80 cells/mm³ and median HIV RNA of 91 800 copies/mL. Malnutrition, opportunistic infections, and sarcopenia were observed in 32% ($n=16$), 22% ($n=11$), and 14% ($n=7$) of patients, respectively. Altogether, mortality was 24% (12/50), with 75% of deaths occurring within first three months and a median time to death of 31 days. Among survivors, median CD4 count escalated from 93 to 236 cells/mm³, and almost all were virally suppressed by month nine. Prognostic factors of mortality involved severe malnutrition, sarcopenia, hypoalbuminaemia, CD4 count below 50 cells/mm³, viral load exceeding 100 000 copies/mL, and multi-organ abnormalities at presentation.

Conclusions: Locally produced integrase inhibitor-based ART achieved excellent responses in survivors with advanced HIV disease. Early mortality was high. Poor nutritional status, sarcopenia,

severe immunosuppression, and multi-organ involvement were significantly related to mortality. This highlights the urgent need for earlier HIV diagnosis, proper nutritional screening and intervention, and management of opportunistic infections in developing countries as in Egypt.

Summary

Question: What clinical, immunological, virological, and nutritional outcomes follow locally manufactured dolutegravir-based therapy in treatment-naïve adults with advanced HIV disease, and what factors predict early mortality?

Findings: In this prospective cohort of 50 treatment-naïve patients, early mortality was 24% (median survival, 31 days), while all 38 survivors achieved viral suppression by nine months with marked immunological and nutritional recovery. Severe malnutrition, sarcopenia, hypoalbuminemia, CD4 count below 50 cells/mm³, and viral load above 100 000 copies/mL predicted mortality.

Meaning: Locally manufactured dolutegravir-based ART yields excellent outcomes in survivors with advanced HIV disease, but early mortality remains high, underscoring the need for earlier HIV diagnosis and structured baseline risk assessment.

✉To whom correspondence may be addressed. E-mail: ayaelsheef1@gmail.com

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1. Introduction

HIV has been a global health issue. It affects approximately 39 million people with nearly 1.3 million newly discovered persons with infections every year. With advancement of antiretroviral therapy (ART) and its early initiation, the disease progression and consequently the mortality had improved dramatically. Despite all these measures, certain percentage of people, especially in low- and middle-income areas, still present with advanced HIV disease (AHD) at the time of diagnosis or treatment initiation[1].

AHD is defined by a CD4 T cell count below 200 cells/mm³ or the presence of an AIDS-defining illness. Despite the remarkable improvement in HIV care, AHD is still frequent even in high-income settings, where around one in three new cases presents at advanced stage[2]. People with AHD face seriously worse outcomes and frequent co-concomitant of opportunistic infections leading to high morbidity and mortality[3]. Nevertheless, robust long-term outcome data for this population remain scarce[4].

To date, no prospective study from the Middle East and North Africa (MENA) region has examined outcomes of generic, locally manufactured integrase strand transfer inhibitor (INSTI)-based ART in treatment-naïve patients presenting with AHD. The comparative effectiveness of different antiretroviral strategies, particularly boosted protease inhibitor (PI/b)-based versus INSTI-based regimens, in this specific population remains poorly characterized[5].

Current international guidelines recommend regimens with a higher genetic barrier, such as PI/b or second-generation INSTIs, to enable immediate treatment initiation prior to receiving genotypic resistance testing results[6]. Early investigations into INSTI-based approaches, notably those incorporating raltegravir (RAL) within four-drug or five-drug intensified regimens, failed to demonstrate meaningful mid- or long-term advantages over standard ART[7]. More recent evidence, however, suggests that triple INSTI-based regimens used as initial therapy offer good efficacy and tolerability, with faster rates of viral suppression and immune recovery compared to PI/b regimens[8].

Aligned with these findings, Egypt's Ministry of Health had revised its National AIDS Program guidelines in 2021, declaring that the combination of tenofovir disoproxil fumarate (TDF), emtricitabine (FTC), and dolutegravir (DTG) is the preferred first-line ART regimen for adults[9].

Apart from virological and immunological issues, malnutrition constitutes one of the considerable and usually underestimated complications in AHD[10]. People who presented with significant weight loss exceeding 5% of body weight have a higher risk of

accelerated disease progression, weakened physical function, and increased mortality risk. In resource-limited regions, a low body mass index (BMI below 18 kg/m²) at ART initiation is considered a strong independent predictor of early death within the first six months of treatment[11]. Sarcopenia is defined as a concurrent loss of muscle mass and impaired muscle function, according to the European Working Group on Sarcopenia in Older People (EWGSOP), is ever more documented among people living with HIV (PLHIV)[12]. Regardless of ART use reduced wasting and mortality, sarcopenia is frequently observed in PLHIV. The prevalence is comparable to that observed in other chronic diseases. This condition leads to disability, falls, fractures, and premature death, emphasizing the need for early detection and integrated management strategies[13]. Routine monitoring of anthropometric measures, including body weight, BMI, and mid-upper arm circumference (MUAC), is consequently essential in individuals with AHD[14].

The prognostic nutritional index (PNI), derived from serum albumin levels (a marker of nutritional status) and lymphocyte count (a marker of immune function), has demonstrated utility as a prognostic tool across a range of chronic diseases[15]. However, its value as a predictive marker in AHD has yet to be prospectively validated in the MENA context, representing an important gap in the existing evidence base.

This study therefore aimed to: (1) evaluate clinical, immunological, virological, and nutritional responses to locally manufactured generic DTG-based ART over nine months in treatment-naïve adults with AHD at a tertiary HIV clinic in Egypt; (2) identify baseline prognostic factors associated with early mortality in this population; and (3) assess the feasibility and effectiveness of generic INSTI-based regimens as a model for AHD management in resource-limited settings.

2. Methods

2.1. Study design

We conducted a prospective longitudinal cohort study at the HIV Clinic, Kasr Al-Ainy Hospital, Cairo University between March 2023 and August 2024. The study enrolled ART-naïve adults presenting with AHD.

2.2. Inclusion and exclusion criteria

Eligible participants were adults (aged ≥18 years) who were ART-naïve and met the World Health Organization (WHO) definition for AHD: either a CD4 count ≤200 cells/mm³ (regardless of clinical stage) or the presence of an AIDS-defining illness at any CD4 count. All participants were required to provide informed consent and

commit to the follow-up schedule.

Patients who otherwise met the inclusion criteria were excluded if they were pregnant or lactating at the time of enrollment.

2.3. Treatment regimen

All participants were initiated on INSTI-based antiretroviral therapy following national guidelines. The standard regimen consisted of generic locally manufactured dolutegravir 50 mg once daily plus tenofovir disoproxil fumarate/emtricitabine (300/200 mg) once daily. The locally manufactured dolutegravir (DTG) formulation was produced under licensing agreements with the Egyptian Ministry of Health. Although formal bioequivalence testing for this specific batch was not independently conducted within our study, the product has received approval from national regulatory authorities and has been incorporated into Egypt's national treatment program since 2021. Treatment adherence was assessed at each follow-up visit using patient self-report of missed doses in the preceding 30 days and categorized as good (≤ 1 missed dose per month), fair (2–4 missed doses per month), or poor (> 5 missed doses per month).

2.4. Sample size

With a sample size of at least 50, we had a power of 90% to assess whether the response rate in patients receiving generic integrase inhibitors (~90%) using a one sample proportion test and a significance level of 0.05. The following formula was used for the sample size n :

$n = N * X / (X + N - 1)$, where, $X = Z_{\alpha/2}^2 * p(1-p) / MOE^2$, and $Z_{\alpha/2}$ is the critical value of the normal distribution at $\alpha/2$ (e.g. for a confidence level of 95%, α is 0.05 and the critical value is 1.96), MOE is the margin of error, p is the sample proportion, and N is the population size.

2.5. Data collection and follow-up schedule

Participants underwent comprehensive clinical assessment at four time points: baseline (ART initiation), 3 months, 6 months, and 9 months post-ART initiation. At each visit, standardized case report forms were used to collect the following data: (1) Demographic information; (2) HIV-specific data: Date of diagnosis, WHO clinical stage, nadir CD4 count, HIV RNA viral load, current ART regimen, treatment adherence; (3) Clinical assessment; (4) Anthropometric measurements; (5) Laboratory testing; and (6) Imaging studies.

2.6. Clinical and laboratory assessment

2.6.1. Anthropometric measurements

All anthropometric measurements were performed in triplicate

by trained personnel following standardised protocol, with mean value used in subsequent analyses. BMI was calculated using the standard formula: weight (kg) divided by height squared (m^2). Waist circumference was measured at the midpoint between the lower costal margin and the iliac crest. Mid-upper arm circumference (MUAC) was assessed at the midpoint between the acromion and olecranon processes; values below 23 cm in males and 22 cm in females were used as thresholds to identify malnutrition risk.

Sarcopenia was defined in accordance with the European Working Group on Sarcopenia in Older People (EWGSOP) criteria, requiring concurrent presence of reduced muscle mass and impaired muscle function. Muscle strength was assessed using a handheld dynamometer, with the highest value recorded across six measurements, three per hand, expressed in kilograms. Given the resource-limited setting of this study, MUAC was employed as a validated proxy measure for muscle mass in place of the criterion-standard modalities recommended by EWGSOP, namely dual-energy X-ray absorptiometry (DEXA) or bioelectrical impedance analysis (BIA)[14]. While use of MUAC as a surrogate is well-supported in the literature for such contexts, this represents a methodological limitation that may introduce some degree of misclassification, and is acknowledged accordingly. Full measurement protocols are detailed in Supplementary Methods S1.

2.6.2. Laboratory methods

Blood samples were collected after 8–12 hours of fasting. CD4 T-cell counts were measured by flow cytometry, and HIV-1 RNA viral load by real-time PCR, with viral suppression defined as HIV RNA below the lower limit of quantification. Complete blood counts, serum albumin, liver enzymes (AST, ALT), total bilirubin, creatinine, lipid profiles, and hemoglobin A1c were measured using standard automated analyzers. Detailed laboratory methods are provided in Supplementary Methods S2.

2.6.3. Imaging assessment

All participants underwent baseline abdominal ultrasonography. Computed tomography of chest and/or abdomen was performed when clinically indicated (suspected opportunistic infections, unexplained organomegaly, persistent fever, or respiratory symptoms). Hepatic fibrosis and steatosis were longitudinally evaluated using transient elastography (FibroScan): Liver stiffness measurements (KPA) were utilized to determine fibrosis staging, while Controlled Attenuation Parameter (CAP) scores were utilized to assess steatosis stages across the follow-up period. Findings were systematically recorded from radiology reports using standardized forms. Detailed imaging protocols are provided in Supplementary Methods S3.

2.7. Statistical analysis

Baseline characteristics were summarised using frequencies and percentages for categorical variables, and either means with standard deviations or medians with interquartile ranges for continuous variables, depending on the normality of their distribution. Between-group comparisons of survivors and non-survivors were conducted using *Chi-square* or Fisher's exact tests for categorical variables, and independent samples *t*-tests or Mann-Whitney *U* tests for continuous variables, as appropriate.

Longitudinal changes in continuous outcomes were modelled using linear mixed-effects models (LMER), incorporating time as a fixed effect and participant-level random intercepts to account for within-subject correlation. For binary longitudinal outcomes, specifically muscle strength recovery and virological suppression, generalised linear mixed-effects models (GLMER) were fitted using a binomial distribution with a logit link function. All models were adjusted for age, sex, baseline CD4 count, BMI, and AIDS diagnosis status. Predicted probabilities with 95% confidence intervals (CIs) were derived and plotted across time points. Participants who died during follow-up were excluded from longitudinal analyses to ensure that treatment response trajectories reflected outcomes in survivors only.

Time-to-event analyses were performed using the Kaplan-Meier method. Survival curves were constructed for overall mortality, AIDS-related mortality, and time to first hospitalisation. Continuous prognostic factors were stratified either by median values, such as PNI below versus at or above 43.5, or according to clinically established thresholds, such as CD4 count below versus at or above 100 cells/mm³. Between-group differences in survival distributions were assessed using log-rank tests, and median survival times with 95% CIs were reported where estimable. Follow-up duration was calculated from the date of ART initiation to the date of death, loss to follow-up, or study completion, whichever occurred first.

All statistical analyses were conducted using R software (version 4.3), with a two-sided significance threshold of $P < 0.05$. Patterns of missing data were examined and documented. Longitudinal analyses utilised all available data under the missing-at-random assumption. Given the limited sample size, full multivariable modelling was not pursued, as the number of observed events did not meet the recommended threshold of 10 to 15 events per variable required for reliable model estimation.

2.8. Ethics approval

Written informed consent was obtained from all participants prior to enrolment; no participants required a consent exemption. The study was approved by the Institutional Review Board of Cairo University (IRB approval number: 114-2023; approval date: 1/10/2023), and all study procedures were conducted in accordance with the ethical principles of the Declaration of Helsinki.

3. Results

3.1. Patient characteristics

Between March 2023 and August 2024, a total of 62 treatment-naïve adults presenting with AHD were initially evaluated at the clinic. Of these, 12 individuals were excluded as they did not meet the eligibility requirements, leaving 50 patients who fulfilled all inclusion criteria and were enrolled in the study. All participants initiated generic dolutegravir-based antiretroviral therapy and were followed for up to 9 months. Twelve participants (24%, 12/50) died over the course of the study. All 38 surviving participants completed the 9-month follow-up period, yielding a 100% retention rate among survivors with no loss to follow-up.

Baseline characteristics are summarised in Table 1. The mean age was (37.6 ± 10.2) years, and the majority were male (76%, $n=38$). The median baseline CD4 count was 80.0 cells/mm³, and the median HIV RNA viral load (PCR) was 91800 copies/mL, reflecting a wide range of virological burden. As regards nutritional and physical health, the mean PNI was 42.6, the median BMI was 22.0 kg/m² (IQR: 19.8–23.9), and 14% ($n=7$) of the group met the criteria for sarcopenia. Additionally, 22% of subjects presented with opportunistic infections at enrollment.

Regarding overall treatment adherence, 78% of our cohort demonstrated good adherence, defined by missing one or fewer doses per month, 16% reported fair adherence, defined as missing two to four doses per month, and 6% were classified as having poor adherence, defined as missing more than five doses per month.

With respect to inpatient care, 20 patients (40%) had at least one hospital admission. The median duration of admission was 10 days (IQR: 7–14). The leading causes for admission were dyspnea reported in 5 cases (25%, 5/20) followed by anemia (20%), accounting for 4 admissions. Among the reported AIDS-defining conditions in this cohort, recurrent bacterial infections were the most frequent, observed in 6 individuals (30%), followed by *Mycobacterium tuberculosis* (25%) and lymphoma (15%).

3.2. Prognostic factors for early mortality in advanced HIV group

Mortality was 24% (12 participants), with a median time to death of 31 days (IQR: 22.5–68.5); Nine of twelve deaths (75%) occurred within the first three months of treatment due to AIDS-related illnesses. Table 2 presents a comparative analysis of baseline characteristics and clinical parameters between survivors ($n=38$) and non-survivors ($n=12$). Several prognostic factors were significantly associated with early mortality.

An AIDS diagnosis at baseline was strongly linked to death (75.0% *vs.* 26.3%; $P < 0.01$). Non-survivors also had significantly lower MUAC (23.6 *vs.* 27.0 cm; $P < 0.001$) and BMI (19.1 *vs.* 23.0 kg/m²; $P < 0.01$). Sarcopenia was present in 33.4% of non-survivors compared with 7.9% of survivors ($P < 0.05$). In addition, nonsurvivors demonstrated markedly reduced albumin levels (2.98

vs. 3.98 g/dL; $P<0.001$), hemoglobin concentrations (9.68 vs. 12.1 g/dL; $P=0.01$), and PNI scores (33.6 vs. 45.5; $P<0.001$). Median viral load was substantially higher in non-survivors [3 000 000 (IQR: 1 027 500–7 625 000) vs. 15 000 (IQR: 3 888–322 000) copies/mL; $P=0.005$. Although CD4 category did not reach statistical significance ($P=0.13$), likely due to limited statistical power, 58.3% of non-survivors had CD4 <50 cells/mm³, compared with 23.7% of survivors, representing a clinically important difference that warrants attention in larger studies. Additional details are shown in Supplementary Table 1.

Table 1. Baseline characteristics of the advanced HIV cohort ($n=50$).

Variable	Data
Age, years, mean $\pm$ SD	37.6 $\pm$ 10.2
Sex, n (%)	
Female	12 (24)
Male	38 (76)
Employment status, n (%)	
Employed/Self-employed	29 (58)
Unemployed	21 (42)
Body mass index, kg/m ² , median (IQR)	22.0 (19.8–23.9)
Sarcopenia, n (%)	7 (14)
Malnutrition, n (%)	
No	34 (68)
Yes	16 (32)
Opportunistic infection at baseline, n (%)	
No	39 (78)
Yes	11 (22)
AIDS at diagnosis, n (%)	19 (38)
Overall treatment adherence, n (%)	
Good (≤ 1 missed dose per month)	39 (78)
Fair (2–4 missed doses per month)	8 (16)
Poor (>5 missed doses per month)	3 (6)
CD4 count at baseline, cells/mm ³ , median (IQR)	80.0 (41.8–130.0)
HIV RNA (PCR) at baseline, copies/mL, median (IQR)	91 800 (5 540–3 000 000)
Prognostic nutritional index, mean $\pm$ SD	42.6 $\pm$ 8.9

3.3. Dynamics of viral suppression

Across the 9-month follow-up period as seen in Figure 1, viral suppression rates were assessed only among patients who remained alive and evaluable at each follow-up. At baseline, none had achieved suppression (0%). By three months, 15.8% ($n=6$) of the 38 surviving evaluable patients were suppressed. This proportion rose to 70.8% (17 of 24) at six months, and by nine months all 38 survivors (100%) had achieved suppression. The pattern reflected a steady and statistically significant improvement over time ($P<0.001$).

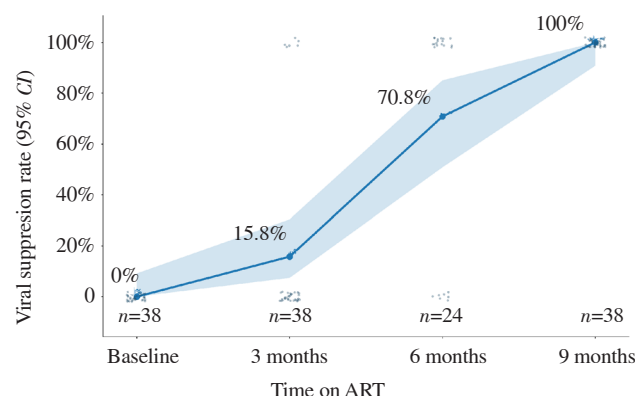


Figure 1. Viral suppression rates over time among treatment-naïve advanced HIV patients initiating antiretroviral therapy. Some data (PCR) was unavailable at 6-month visit due to a temporary shortage of diagnostic kits at this time; however, these patients completed their 9-month visit and achieved viral suppression.

Table 2. Factors associated with early mortality in treatment-naïve advanced HIV patients initiating antiretroviral therapy.

Parameters	ALL ($n=50$)	Alive ($n=38$)	Dead ($n=12$)	P
AIDS diagnosis at baseline, n (%)				
No	31 (62.0)	28 (73.7)	3 (25.0)	<0.01
Yes	19 (38.0)	10 (26.3)	9 (75.0)	
Body mass index, kg/m ² , median (IQR)	22.0 (19.8–23.9)	23.0 (20.2–25.4)	19.1 (17.8–22.0)	<0.01
Malnutrition severity, n (%)				<0.001
None	22 (44.0)	22 (57.9)	0 (0.0)	<0.001
Mild	11 (22.0)	8 (21.1)	3 (25.0)	
Moderate	11 (22.0)	6 (15.8)	5 (41.7)	
Severe	6 (12.0)	2 (5.3)	4 (33.3)	
MUAC, cm, mean $\pm$ SD	26.2 $\pm$ 3.1	27.0 $\pm$ 2.9	23.6 $\pm$ 2.4	<0.001
Sarcopenia, n (%)				<0.05
No	43 (86.0)	35 (92.1)	8 (66.6)	<0.05
Yes	7 (14.0)	3 (7.9)	4 (33.4)	
Viral load, copies/mL, median (IQR)	91 800 (5 540–3 000 000)	15 000 (3 888–322 000)	3 000 000 (1 027 500–7 625 000)	0.005
CD4 category, n (%)				0.13
<50 cells/mm ³	16 (32.0)	9 (23.7)	7 (58.3)	0.13
50–99 cells/mm ³	18 (36.0)	15 (39.5)	3 (25.0)	
100–199 cells/mm ³	16 (32.0)	14 (36.8)	2 (16.7)	
Hemoglobin, g/dL, mean $\pm$ SD	11.50 $\pm$ 2.64	12.10 $\pm$ 2.39	9.68 $\pm$ 2.65	0.01
Albumin, g/dL, mean $\pm$ SD	3.74 $\pm$ 0.74	3.98 $\pm$ 0.60	2.98 $\pm$ 0.63	<0.001
Prognostic nutritional index, mean $\pm$ SD	42.6 $\pm$ 8.9	45.5 $\pm$ 7.2	33.6 $\pm$ 8.0	<0.001

MUAC: mid-upper arm circumference.

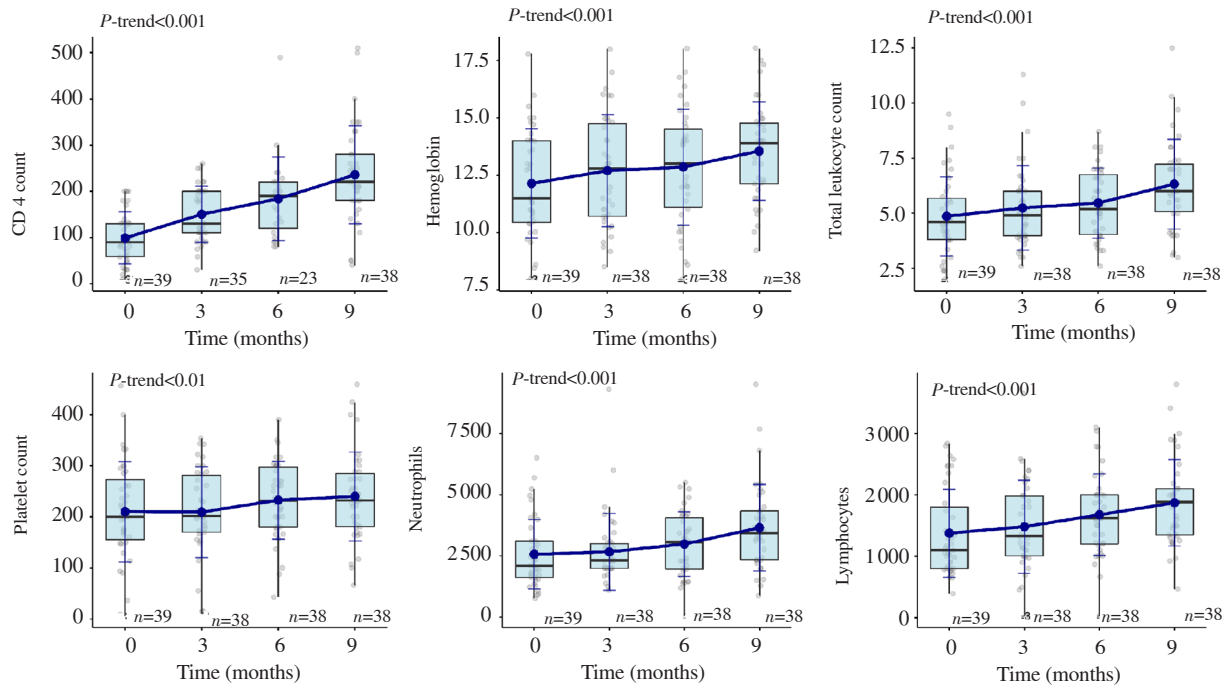


Figure 2. Immuno-hemato parameters over time among treatment-naïve advanced HIV patients initiating ART. Some data (CD4) is unavailable due to a temporary shortage of diagnostic kits.

3.4. Immunological response and clinical outcomes

Immune recovery was evident as illustrated in Figure 2. The median CD4 count enhanced from 93 cells/mm³ at baseline to 236 cells/mm³ by 9 months, and 96.3% of survivors ($n=37$ of 38) achieved a CD4 gain exceeding 100 cells/mm³ (P -trend<0.001). Final follow up of CD4 results were divided into four categories: 36.8% persisted below 200 cells/μL, 55.3% were in the 200-350 cells/μL range, while 5.3% reached 350-500 cells/μL, and only 2.6% exceeded 500 cells/μL, underlining the persistent immunological debit that among those late-presenting individuals.

Univariable analysis shown in Figure 3 identified four statistically significant predictors of immune recovery: higher serum albumin (median 4.0 *vs.* 3.4 g/dL, $P<0.001$), higher hemoglobin (median 12.8 *vs.* 10.6 g/dL, $P<0.01$), younger age (median 33 *vs.* 43 years, $P=0.02$), and lower WHO clinical stage at diagnosis (median 2 *vs.* 3, $P=0.04$). Higher baseline CD4 count showed a trend toward significance (median 90 *vs.* 60 cells/μL, $P=0.05$). Sarcopenia was not significantly associated with immune recovery ($OR=0.34$, $P=0.41$), though the direction of effect suggested a lower likelihood of recovery among sarcopenic patients.

Hemoglobin levels also rose steadily (P -trend<0.001), accompanied by parallel increases in total leukocyte count, neutrophils, and lymphocytes (all P -trend<0.001), suggesting improved hematological function. While other metabolic parameters also showed favorable trends: HbA1c and triglycerides declined

progressively, whereas total cholesterol, low-density lipoprotein (LDL), and high-density lipoprotein (HDL) remained stable as illustrated in Figures 2 and 4.

Significant improvements were observed in key nutritional indicators during the 9-month follow-up period as illustrated in Figure 4. Body weight increased progressively from baseline to 9 months (P -trend<0.001), paralleled by consistent gains in serum albumin (P -trend<0.001) and waist circumference (P -trend < 0.001) reflecting significant nutritional recovery.

Regarding sarcopenia specifically: of the three surviving sarcopenic patients, one resolved sarcopenia by month 3 and all 3 had resolved by month six, demonstrating that ART-driven nutritional and immunological recovery can reverse sarcopenia in survivors. No new (incident) cases of sarcopenia were recorded among the 35 non-sarcopenic survivors at any time point.

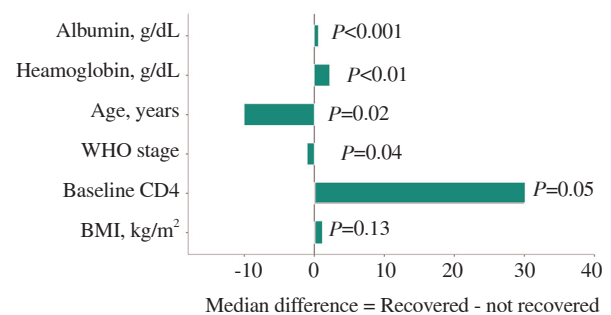


Figure 3. Factors associated with immune recovery in treatment-naïve advanced HIV patients initiating antiretroviral therapy.

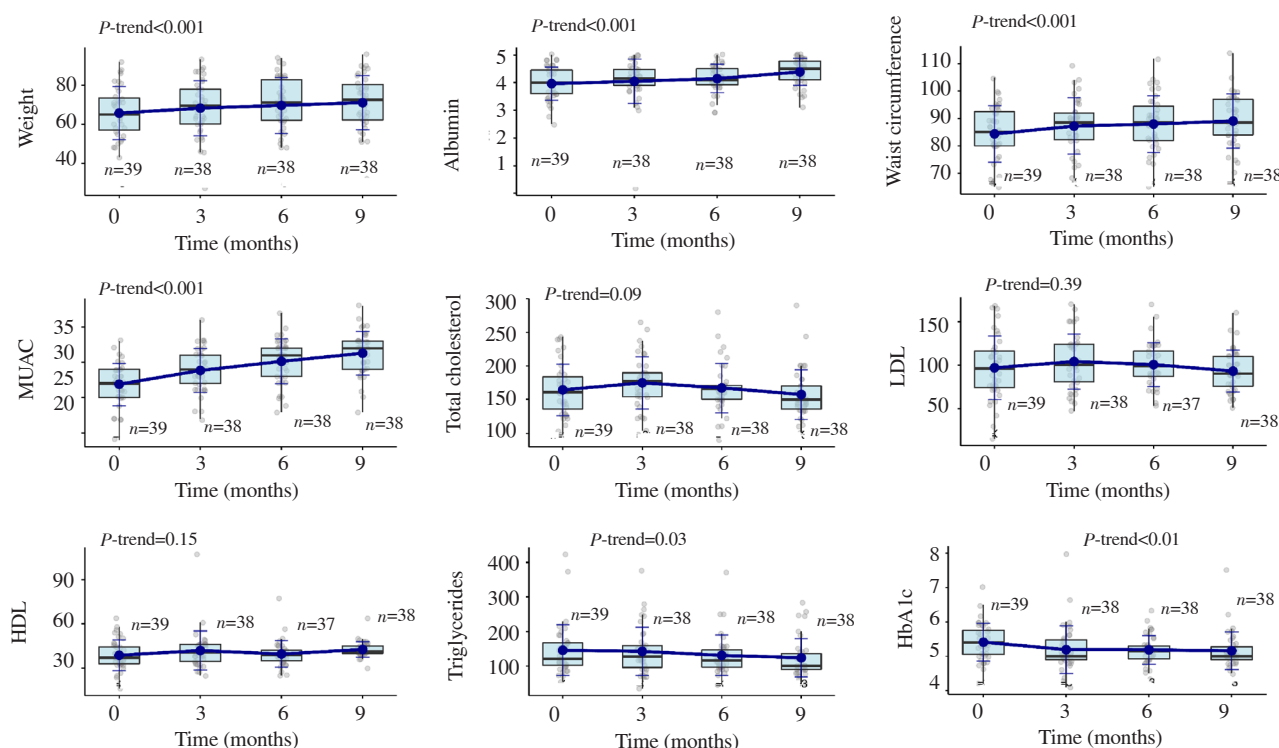


Figure 4. Metabolic parameters over time among treatment-naïve advanced HIV patients initiating ART. Some data (LDL, HDL) are unavailable at 6 months follow up due to a temporary shortage of diagnostic kits at that time. MUAC: mid-upper arm circumference; LDL: low-density lipoprotein; HDL: high-density lipoprotein.

4. Discussion

In this prospective cohort of 50 treatment-naïve adults presenting with AHD who initiated generic, locally manufactured DTG-based ART and were followed up at a tertiary HIV centre in Egypt. Early mortality reached 24%, with 75% of deaths occurring within the initial three months. Encouragingly, among those who survived, 100% attained viral suppression by nine months associated with excellent immunological, nutritional, and functional recovery. This observation highlighting a striking contradiction, effective therapy for survivors beyond the critical post-ART initiation phase, opposed to the distressingly high early mortality affected by the severity of clinical condition at baseline.

We used the DTG-based therapy in this cohort in accordance to an Egyptian national mass shift in 2021. This modification was guided by dolutegravir's excellent genetic barrier, proven efficacy, and favorable tolerability[9]. The demographics of our cohort showed 76% were male, with a mean age of 37.6 years which reflects the Egyptian epidemiological trends. UNAIDS has observed in Egypt that an estimated 27 000 adult men are living with HIV, nearly double the number of involved women. This stood in contrast to the global pattern of female predominance[16]. The high prevalence of men explained by structural and societal barriers. Compared with

women who recognised through routine antenatal screening, men miss systematic entry points and additionally hindered by stigma and the psychological issue of diagnosis, as studied by Lifson *et al.* and Staveteig *et al.*[17,18]. Consequently, men often present with marked immunodeficiency and opportunistic infections with reduced survival. These results are alongside with our earlier research conducted at our center by Al Sehemly *et al.* which observed that young-to-middle-aged males were the prevalent late-presenting group[19].

The significant clinical fragility of this cohort was reflected by the early mortality. Taken together, 24% of participants ($n=12$) died, with 75% occurring in the first three months. The median survival duration was only 31 days. This was precipitated by severe immunosuppression which result in a heavy burden of opportunistic infections and consequently marked nutritional deterioration at presentation. Hospitalization data further confirmed this vulnerability, with 40% of participants requiring at least one inpatient admission. The mean stay was 10.79 days, most often due to dyspnea, anemia, or sepsis.

The mortality rate of our cohort is obviously higher than the 5% observed by Moh *et al.* in an AHD West African cohort[20]. This difference may be explained by variations in clinical status at baseline enrollment rather than by differences in ART regimen

effectiveness. Significantly, the aggregation of early deaths coincides with the findings of Cornell *et al.* who reported that most AHD related mortality occurs within the first four months of ART initiation[21]. This confirmed the importance of the clinical monitoring and prophylactic measures.

Non-survivors exhibited signs of systemic inflammatory collapse at presentation, characterized by severe malnutrition, low BMI, depleted levels of albumin, hemoglobin, and PNI and history of blood transfusion. Severe immunosuppression (CD4 <50 cells/mm³ in 58.3% of non-survivors), and high viral loads were strongly associated with mortality, mirroring findings by Workie *et al.* and Biset[22,23]. This marked immunosuppression facilitates opportunistic infections, documented in 23.5% of our participants with recurrent bacterial infections and *Mycobacterium tuberculosis* being the most prevalent. Tuberculosis, in particular, drives profound anemia which required blood transfusion and hypoalbuminemia; this stems from a combination of poor nutritional intake and the high metabolic load imposed by chronic gastrointestinal and systemic symptoms. These results align with Huang *et al.* confirming that the synergy between malnutrition and infection accelerates disease progression and heightens mortality risk[24].

The significant association between sarcopenia and higher mortality in our cohort aligns with global evidence. Specifically, Liu *et al.* demonstrated in a systematic meta-analysis that frailty, of which sarcopenia is a core component, is associated with a 2.69-fold higher risk of mortality in HIV populations[25]. Furthermore, the independent prognostic significance of PNI aligns with oncological evidence from Sun *et al.* who demonstrated that low PNI was associated with poorer overall survival[26]. This makes it as an excellent marker of both nutritional and immune status in AHD. In addition to our finding about sarcopenia, reduced BMI, anemia, and hypoalbuminemia as prognostic tools of mortality are supported by the results of Liu *et al.* and Huang *et al.*[24,27]. This highlighting the importance of a comprehensive framework for risk stratification at the time of HIV diagnosis and treatment initiation.

Regardless of high early mortality, viral suppression rate raised outstandingly among survivors from 15.8% at three months to 100% by nine months. These results went beyond the what were observed by Setpakdee *et al.* and Gan *et al.* in their cohorts using dolutegravir (DTG) regimen[28,29].

This dramatic 100% suppression rate illuminates the effectiveness of locally manufactured generic dolutegravir. Although there were not possible direct comparisons with other regimens, this progress reminds us with Egypt's breakthrough achievement with generic DAAs for hepatitis C. It proved that affordable, locally produced medicines can act as powerful tools for managing AHD[30].

Encouragingly these excellent consequences were attained with no need for resistance testing or regimen switching. This supports the concept of a 'watchful continuation' approach that

takes the privilege of dolutegravir's effectiveness. This allows slow responders up to nine months to reach suppression and prevent premature modifications to more costly alternatives. Such practice is consistent with current highgeneticbarrier treatment guidelines[6]. It is necessary to acknowledge that, without genotypic resistance testing, true virological failure couldn't be reliably differentiated from delayed suppression[31]. Future researches involving genotypic resistance testing at the threemonth points in unsuppressed patients could make valuable insights.

The outstanding outcomes were led by strong compliance. The 78% of cohort continuing good compliance. This was accompanied by 100% retention over nine months, a remarkable improvement compared with the 70% observed by Cordie *et al.* This mostly attributable to active nursing involvement, comprehensive followup, and the HIV clinic team's unwavering institutional commitment. Eventually, this monitoring approach strengthened adherence and consequently achieve the exceptional viral suppression[32].

Through analysis of immune recovery, over 90% of the survivors' CD4 count didn't reach 350 cells/mm³, and more than onethird stayed under 200 cells/mm³. This observation alongside what Camici *et al.* who reported a mean CD4 rise from 133 to 309 cells/μL by week 48, with 83% of AHD patients surpassing 200 cells/μL, highlighting the concept of incomplete immune recovery despite full virological suppression[33]. This emphasizes that timely HIV diagnosis is critical, as immune debt couldn't be completely restored within nine months. The earlier presenters attain more complete recovery.

Beyond virological and immunological concerns, there were significant advances obtained with nine months of generic DTG-based ART through nutritional, anthropometric, haematological, and metabolic measures. This is inconsistent with PrayGod *et al.* who observed improvements in MUAC, waist circumference, and serum albumin confirmed the fatfree mass increases[34]. All previously sarcopenic individuals had improved sarcopenia by month six, this was associated with functional recovery represented by strengthening of handgrip, consistent with the findings of Filteau *et al.*[35]. Significant haematological improvement was also observed, in line with Sah *et al.*[36]. Additionally, declines in HbA1c and downward trajectory of triglycerides reflected more metabolic control. These findings collectively confirm the comprehensive recovery of the survivors under locally manufactured generic dolutegravir-based therapy.

This study has many key strengths: its prospective design with novel use of multiorgan imaging for risk stratification, thorough clinical evaluations, and validation of locally produced generic dolutegravir in AHD. On the other side, limitations include the modest, singlecenter sample size, with only 12 deaths restricting statistical power and precluding robust multivariable modeling; besides, some social determinants such as stigma and food security were not assessed. Future largescale, multicenter studies with using

of resistance genotyping and structured psychosocial assessments are required to support these findings and inform targeted nutritional and stigma reduction interventions.

In conclusion, advanced HIV disease is still considered a major health burden in Egypt, with majority of deaths occurring in the early phase of ART initiation due to severe immune and nutritional depletion. This study underscores the important role of the structured risk assessment and close monitoring in improving the survival. It also confirms the effectiveness of early generic dolutegravir for achieving viral suppression. Reducing mortality necessitates proactive early monitoring combined with use of generic integrase inhibitors as the cornerstone of care.

Conflict of interest statement

The authors declare no conflicts of interest.

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Authors' contributions

AC and RAA conceived and designed the study. MA collected data and drafted the manuscript. AMK and ZA contributed to data analysis and interpretation. AMA, MBH and RM contributed to participant recruitment, data collection, and clinical management. ZA and HHT performed laboratory and imaging assessments and contributed to data interpretation. AC and LAS supervised the study, contributed to its conception and design, and critically revised the manuscript for important intellectual content. All authors read, critically revised, and approved the final version of the manuscript.

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Supplementary Methods S1: Detailed anthropometric measurement protocols

General procedures

All anthropometric measurements were performed by trained clinical personnel who had completed standardized training in measurement techniques. Participants were measured wearing light indoor clothing without shoes. Each measurement was performed three times consecutively, and the meaning of the three values was calculated and used for analysis. If two measurements differed by more than 0.5 cm (for circumferences) or 0.5 kg (for weight), a fourth measurement was taken and the median value used.

Body mass index (BMI)

Weight was measured using a calibrated digital scale [SPECIFY MODEL IF AVAILABLE] accurate to 0.1 kg. Participants stood in the center of the scale platform without support, with weight distributed evenly on both feet. Height was measured using a stadiometer [SPECIFY IF AVAILABLE] with participants standing erect, heels together, and head positioned in the Frankfurt horizontal plane (lower margin of orbit in same horizontal plane as upper margin of external auditory meatus). Height was recorded to the nearest 0.1 cm. BMI was calculated as weight (kg) divided by height squared (m^2) and categorized according to WHO criteria:

- Underweight: $<18.5 \text{ kg/m}^2$
- Normal weight: $18.5\text{-}24.9 \text{ kg/m}^2$
- Overweight: $25.0\text{-}29.9 \text{ kg/m}^2$
- Obese: $\geq 30.0 \text{ kg/m}^2$

Mid-upper arm circumference (MUAC)

MUAC was measured on the right arm following WHO standardized protocols:

1. **Positioning:** The participant stood upright with the right arm hanging loosely at the side, palm facing the thigh.
2. **Midpoint identification:** The shoulder tip (acromion process) and elbow tip (olecranon process) were palpated and marked. A non-stretchable measuring tape was used to measure the distance between these two points. The midpoint was calculated and marked on the lateral aspect of the arm.
3. **Measurement:** With the arm still hanging loosely, a non-stretchable measuring tape was wrapped horizontally around the arm at the marked midpoint, perpendicular to the long axis of the arm. The tape was positioned snugly but without compressing the soft tissue. The measurement was read at the point where the tape overlapped, recorded to the nearest 0.1 cm.
4. **Interpretation:** MUAC values were classified as:
 - Males: $<23 \text{ cm}$ indicates malnutrition risk; $\geq 23 \text{ cm}$ considered normal
 - Females: $<22 \text{ cm}$ indicates malnutrition risk; $\geq 22 \text{ cm}$ considered normal

References for MUAC cutoffs:

- World Health Organization. *Physical status: the use and interpretation of anthropometry. WHO technical report series 854*. Geneva: WHO; 1995.

- Tang AM, Dong K, Deitchler M, Chung M, Maalouf-Manasseh Z, Tumilowicz A, et al. Use of cutoffs for mid-upper arm circumference (MUAC) as an indicator or predictor of nutritional and health-related outcomes in adolescents and adults: A systematic review. Washington, DC: FHI 360/FANTA; 2013.

Waist circumference

Waist circumference was measured according to WHO protocols:

1. **Participant preparation:** Participants stood with feet approximately 25-30 cm apart, weight evenly distributed, and arms folded across the chest or hanging loosely at the sides. The abdomen was exposed from just above the iliac crests to just below the costal margin.
2. **Anatomical landmarks:** The lowest point of the lower rib margin (10th rib) and the highest point of the iliac crest were palpated and identified on both sides.
3. **Measurement point:** The measuring tape was positioned horizontally at the approximate midpoint between these two landmarks, typically at the level of the umbilicus. The tape was parallel to the floor and snug without compressing the skin.
4. **Timing:** The measurement was taken at the end of a normal expiration, with the participant breathing normally (not holding breath or forcefully exhaling).
5. **Reading:** The measurement was read to the nearest 0.1 cm at the point of tape overlap.
6. **Interpretation:** Values were classified based on metabolic risk criteria:
 - Males: <94 cm normal; ≥94 cm elevated risk
 - Females: <80 cm normal; ≥80 cm elevated risk

Reference:

- WHO. Waist circumference and waist-Hip ratio: Report of a WHO expert consultation. Geneva, Switzerland: WHO; 2008.

Muscle strength assessment (Grip strength)

Grip strength was measured using a calibrated Jamar-type handheld hydraulic dynamometer [SPECIFY EXACT MODEL AND MANUFACTURER IF KNOWN, e.g., "Jamar Plus+ Digital Hand Dynamometer, Sammons Preston, Bolingbrook, IL, USA" or alternative brand].

Protocol:

1. **Calibration:** The dynamometer was calibrated according to manufacturer specifications at the beginning of each assessment day.
2. **Participant positioning:**
 - Seated in a straight-backed chair
 - Shoulders adducted and in neutral rotation
 - Elbow flexed to 90°
 - Forearm in neutral position (thumb pointing upward)
 - Wrist in neutral position (0-30° extension)
3. **Handle adjustment:** The dynamometer handle was adjusted to fit the participant's hand size, typically with the middle phalanx of the middle finger positioned comfortably on the handle.

4. **Instructions:** Participants were instructed to "squeeze as hard as you can" and were given standardized verbal encouragement without physical contact.
5. **Test procedure:**
 - Three trials performed with the right hand
 - Three trials performed with the left hand
 - Alternating between hands with 60-second rest periods between trials
 - Each squeeze lasted 3-5 seconds
6. **Recording:** All six readings were recorded in kilograms (kg). The highest value among all six readings was selected as the final result for analysis.
7. **Clinical categorization:** In addition to quantitative grip strength, clinical muscle power was assessed by trained physicians using standardized neurological examination techniques and graded according to Medical Research Council (MRC) criteria. For the purposes of this study, clinical muscle power was categorized as:
 - **Weak:** MRC grade ≤ 3 or grip strength below age/sex-specific reference values
 - **Normal:** MRC grade 4-5 and grip strength within normal range
 - **Strong:** MRC grade 5 and grip strength above normal range

Sarcopenia was defined according to the European Working Group on Sarcopenia in Older People (EWGSOP) as the co-occurrence of reduced muscle power (grip strength classified as (weak) AND mid-upper arm circumference (MUAC) below the standard cut-off of 23.5 cm, both assessed at the baseline visit.

Reference:

- Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Yves Boirie, Tommy Cederholm, Francesco Landi, et al. Sarcopenia: European consensus on definition and diagnosis: Report of the European working group on Sarcopenia in older people. *Age Ageing* 2010; 39(4): 412-423.

Quality control

All measurement equipment was calibrated monthly. Inter-rater reliability was assessed during training, with at least 90% agreement required between trainees and the reference measurer before independent data collection. A random sample of 10% of measurements was repeated by a second trained measurer to monitor ongoing measurement quality.

Supplementary methods S2: Detailed laboratory methods

Sample collection and processing

Venous blood samples were collected after an 8-12 hour overnight fast. Participants were instructed to avoid strenuous exercise for 24 hours prior to blood collection. Samples were collected by trained phlebotomists using standard venipuncture techniques between 7:00-10:00 AM to minimize diurnal variation.

Sample tubes and volumes:

- EDTA tube (purple top): 4 mL for complete blood count and CD4 count
- Serum separator tube (gold/red top): 5 mL for chemistry panel, lipids
- Sodium fluoride tube (gray top): 2 mL for glucose/HbA1c
- EDTA plasma tube: 3 mL for HIV viral load (frozen within 6 hours if not processed immediately)

CD4+ T-Cell Enumeration

Method: Flow cytometry using [SPECIFY: e.g., "BD FACSCCount system (Becton Dickinson, Franklin Lakes, NJ, USA)" OR "CyFlow Counter (Sysmex Partec, Görlitz, Germany)" OR "Pima CD4 Analyzer (Abbott, Chicago, IL, USA)"]

Procedure:

1. Whole blood (50 μ L) was added to tubes containing fluorochrome-conjugated monoclonal antibodies (CD3, CD4, CD8)
2. Samples were incubated in the dark at room temperature for 15 minutes
3. Red blood cells were lysed using [SPECIFY lysing solution]
4. Samples were analyzed within 6 hours of collection
5. Absolute CD4 count was calculated automatically by the instrument

Quality control:

- Daily calibration using manufacturer-provided beads
- Commercial quality control materials run with each batch
- Participation in external quality assurance program [SPECIFY if applicable]

Reporting range: 0-3,000 cells/mm³ (or cells/ μ L)

Clinical categories used:

- Severe immunosuppression: <50 cells/mm³
- Advanced immunosuppression: 50-199 cells/mm³
- Moderate immunosuppression: 200-349 cells/mm³
- Mild immunosuppression: 350-499 cells/mm³
- Normal: $\geq$ 500 cells/mm³

HIV-1 RNA Viral Load Quantification

Method: Real-time polymerase chain reaction (RT-PCR)

Platform: [SPECIFY ONE:

- "COBAS AmpliPrep/COBAS TaqMan HIV-1 Test v2.0 (Roche Diagnostics, Basel, Switzerland)"
- "Abbott RealTime HIV-1 assay (Abbott Laboratories, Des Plaines, IL, USA)"
- "Xpert HIV-1 Viral Load (Cepheid, Sunnyvale, CA, USA)"
- "VERSANT HIV-1 RNA 1.0 Assay (kPCR) (Siemens Healthcare Diagnostics, Tarrytown, NY, USA)"
- Or another platform used]

Procedure:

1. Plasma was separated from EDTA whole blood within 6 hours of collection
2. If not tested immediately, plasma was frozen at -70°C
3. Samples were processed according to manufacturer protocol
4. Automated extraction, amplification, and detection

Assay characteristics:

- Lower limit of detection (LLOD): [SPECIFY: typically, 20-40 copies/mL]
- Lower limit of quantification (LLOQ): [SPECIFY: typically, 20-50 copies/mL]
- Upper limit of quantification: [SPECIFY: typically, 10,000,000 copies/mL]
- Linear range: [SPECIFY based on platform]

Definitions:

- **Viral suppression:** HIV RNA below the LLOQ (reported as "undetectable" or "target not detected")
- **Detectable but not quantifiable:** HIV RNA detected but below LLOQ
- **Virological failure:** HIV RNA $\geq 1,000$ copies/mL on two consecutive measurements after initial suppression OR inability to achieve suppression after 6 months of ART

Quality control:

- Manufacturer-provided positive and negative controls run with each batch
- Low, medium, and high-level quality control samples
- Participation in external proficiency testing program

Hematological Analyses

Complete Blood Count (CBC) with Differential

Instrument: [SPECIFY: e.g., "Sysmex XN-1000 (Sysmex Corporation, Kobe, Japan)" OR "Beckman Coulter DxH 800 (Beckman Coulter, Brea, CA, USA)" OR other]

Method: Automated impedance and optical flow cytometry

Parameters measured:

- Hemoglobin (Hb): g/dL
- Hematocrit (Hct): %
- Red blood cell count (RBC): $\times 10^6 / \mu\text{L}$
- Mean corpuscular volume (MCV): fL
- Mean corpuscular hemoglobin (MCH): pg
- Mean corpuscular hemoglobin concentration (MCHC): g/dL
- Red cell distribution width (RDW): %
- White blood cell count (WBC): $\times 10^3 / \mu\text{L}$
- Platelet count (PLT): $\times 10^3 / \mu\text{L}$
- Neutrophils: $\times 10^3 / \mu\text{L}$ and %
- Lymphocytes: $\times 10^3 / \mu\text{L}$ and %
- Monocytes: $\times 10^3 / \mu\text{L}$ and %
- Eosinophils: $\times 10^3 / \mu\text{L}$ and %
- Basophils: $\times 10^3 / \mu\text{L}$ and %

Quality control:

- Three-level quality control materials run daily
- Calibration performed according to manufacturer schedule
- Delta checks comparing current to previous results

Anemia classification:

- Normal: Males ≥ 13 g/dL, Females ≥ 12 g/dL
- Mild anemia: Males 11-12.9 g/dL, Females 11-11.9 g/dL
- Moderate anemia: 8-10.9 g/dL
- Severe anemia: < 8 g/dL

Cytopenia definitions:

- Leukopenia: WBC $< 3,000 / \mu\text{L}$
- Neutropenia: Absolute neutrophil count (ANC) $< 1,500 / \mu\text{L}$
- Lymphopenia: Absolute lymphocyte count $< 1,000 / \mu\text{L}$
- Thrombocytopenia: Platelet count $< 100,000 / \mu\text{L}$ (severe: $< 50,000 / \mu\text{L}$)

Biochemical analyses

Chemistry analyzer: [SPECIFY: e.g., "Roche Cobas c501 (Roche Diagnostics, Basel, Switzerland)" OR "Abbott Architect c8000 (Abbott Laboratories, Abbott Park, IL, USA)" OR other]

Serum albumin

- Method: Bromocresol green (BCG) dye-binding method
- Reference range: 3.5-5.5 g/dL
- Hypoalbuminemia defined as < 3.5 g/dL

Liver function tests

- **Aspartate aminotransferase (AST):**

- Method: Enzymatic rate method (IFCC)
- Reference range: 5-40 U/L
- **Alanine aminotransferase (ALT):**
 - Method: Enzymatic rate method (IFCC)
 - Reference range: 7-56 U/L
- **Total Bilirubin:**
 - Method: Diazo method
 - Reference range: 0.1-1.2 mg/dL

Renal function

- **Serum creatinine:**
 - Method: Enzymatic method (creatinase) or Jaffé method
 - Reference range: Males 0.7-1.3 mg/dL, Females 0.6-1.1 mg/dL
- **Estimated GFR (eGFR):** Calculated using CKD-EPI equation

Lipid profile

Preparation: Fasting for 8-12 hours required

Parameters measured:

- **Total cholesterol:** Enzymatic colorimetric method
- **Triglycerides:** Enzymatic colorimetric method
- **HDL cholesterol:** Direct measurement after selective precipitation
- **LDL cholesterol:** Calculated using Friedewald equation when triglycerides <400 mg/dL; direct measurement when ≥400 mg/dL
 - Friedewald equation: $LDL = Total\ Cholesterol - HDL - (Triglycerides/5)$

Reference ranges:

- Total Cholesterol: <200 mg/dL desirable
- Triglycerides: <150 mg/dL normal
- HDL: >40 mg/dL (males), >50 mg/dL (females) desirable
- LDL: <100 mg/dL optimal

Hemoglobin A1c (HbA1c)

Method: [SPECIFY: e.g., "High-performance liquid chromatography (HPLC)" OR "Immunoturbidimetric assay" OR "Boronate affinity chromatography"]

Instrument: [SPECIFY if known]

Interpretation:

- Normal: <5.7%
- Prediabetes: 5.7-6.4%
- Diabetes: ≥6.5%

Laboratory safety and quality assurance

All laboratory testing was performed by certified medical laboratory scientists in [SPECIFY: e.g., "a CAP-accredited laboratory" OR "a laboratory certified by the Egyptian Ministry of Health" OR other]. Standard operating procedures were followed for all assays. Internal quality control materials were run with each batch of patient samples. The laboratory participated in [SPECIFY external quality assurance programs if applicable].

Reference intervals

All reference intervals were established by the performing laboratory using appropriate reference populations or validated from manufacturer-provided data. Age and sex-specific reference ranges were used when applicable.

Supplementary methods S3: Detailed imaging protocols

Abdominal ultrasonography

Indications: Performed on all participants at baseline as part of routine evaluation for advanced HIV disease.

Equipment: [SPECIFY: e.g., "Philips EPIQ 5 ultrasound system (Philips Healthcare, Amsterdam, Netherlands)" OR "GE LOGIQ E9 (GE Healthcare, Chicago, IL, USA)" OR other]

Transducers: Curvilinear probe, 2-5 MHz or 3.5 MHz

Patient preparation:

- Fasting for at least 6 hours prior to examination
- Full bladder requested (500 mL water 1 hour before exam)
- Supine position, with additional positioning (left lateral decubitus, right lateral decubitus) as needed for optimal visualization

Examination protocol:

1. Liver assessment:

- Size: Measured in midclavicular line from superior to inferior margin
- Normal: <15-16 cm; Hepatomegaly: >16 cm
- Echogenicity: Compared to right kidney cortex
 - Normal: Liver slightly more echogenic than kidney
 - Bright liver/increased echogenicity: Diffusely increased echogenicity (fatty infiltration)
 - Fibrofatty changes: Increased echogenicity with heterogeneous texture
- Contour: Smooth vs. nodular
- Focal lesions: Location, size, echogenicity documented

2. Spleen assessment:

- Size: Measured in longitudinal dimension
- Normal: <12-13 cm; Splenomegaly: >13 cm
- Echogenicity: Homogeneous vs. heterogeneous
- Focal lesions documented if present

3. Kidney assessment:

- Size: Measured in longitudinal dimension (both kidneys)
- Normal: 9-12 cm; Enlarged: >12 cm
- Echogenicity: Cortical echogenicity compared to liver
- Hydronephrosis: Graded as mild, moderate, or severe
- Focal lesions documented if present

4. Lymph node assessment:

- Location: Porta hepatis, para-aortic, mesenteric
- Size: Measured in short axis
- Lymphadenopathy defined as: Short axis >10 mm
- Morphology: Round vs. oval, hilum preservation

5. Other findings:

- Ascites: Presence and estimated volume
- Gallbladder: Wall thickness, stones, polyps
- Pancreas: Size, echogenicity if visualized
- Bowel: Wall thickening if present

Image documentation:

- Representative images saved in DICOM format
- Minimum 3 images per organ
- Measurements recorded on images
- Standardized reporting template used

Reporting:

- All examinations interpreted by board-certified radiologists [SPECIFY: e.g., "with minimum 5 years' experience" OR "fellowship-trained in abdominal imaging"]
- Reports generated using standardized template
- Findings extracted by study personnel using standardized data collection forms

Computed tomography (CT)

Indications: CT of chest and/or abdomen with IV contrast performed when clinically indicated:

- Suspected pulmonary opportunistic infections (tuberculosis, *Pneumocystis jirovecii* pneumonia)
- Unexplained hepatosplenomegaly on ultrasound
- Persistent fever (>7 days) despite empiric antibiotic therapy
- Unexplained respiratory symptoms (cough, dyspnea, hemoptysis)
- Suspected malignancy (lymphoma, Kaposi sarcoma)
- Abdominal pain or symptoms requiring further evaluation
- Abnormal chest radiograph findings

Equipment: [SPECIFY: e.g., "Siemens SOMATOM Definition AS+ (Siemens Healthineers, Erlangen, Germany)" OR "GE Revolution CT (GE Healthcare, Chicago, IL, USA)" OR other]

Patient preparation:

- Fasting 4-6 hours for abdomen/pelvis CT
- Oral contrast: [SPECIFY: e.g., "900 mL of dilute gastrografin or water"] administered 1 hour before scan for abdominal imaging
- IV access: 18–20-gauge peripheral IV catheter
- Renal function screening: Serum creatinine checked; eGFR >30 mL/min/1.73m² required for IV contrast
- Pregnancy test for women of childbearing age

Contrast protocol:

Intravenous contrast:

- Agent: [SPECIFY: e.g., "Iohexol (Omnipaque 350 mg I/mL, GE Healthcare)" OR "Iopromide (Ultravist 370 mg I/mL, Bayer)" OR other]
- Volume: Weight-based dosing [SPECIFY: e.g., "1.5 mL/kg, maximum 150 mL"]
- Injection rate: [SPECIFY: e.g., "3-4 mL/second"]
- Timing: Portal venous phase (60-70 seconds post-injection) for routine abdominal imaging

CT chest protocol:

Scanning parameters:

- Patient position: Supine, arms raised above head
- Scan range: Lung apices through upper abdomen (including adrenal glands)
- Slice thickness: [SPECIFY: e.g., "1-2 mm for lung windows, 5 mm for mediastinal windows"]
- kVp: [SPECIFY: e.g., "120 kVp"]
- mAs: Adjusted based on patient size and automatic dose modulation
- Pitch: [SPECIFY: e.g., "1.0-1.5"]
- Reconstruction: Both lung (high-resolution) and soft tissue (mediastinal) windows

Imaging protocol:

- Non-contrast scan if evaluating for calcifications or hemorrhage
- Contrast-enhanced scan (arterial phase at 25-30 seconds, venous phase at 60-70 seconds) if indicated

Image interpretation - Chest:

- 1. Lungs:**
 - Nodules: Size, location, density (solid, ground-glass, part-solid), number
 - Consolidation: Distribution, air bronchograms
 - Ground-glass opacities: Distribution, pattern
 - Interstitial patterns: Reticular, nodular, mixed
 - Cavitations: Size, wall thickness
 - Effusions: Presence and volume estimation
- 2. Mediastinum:**
 - Lymph nodes: Location, size (short axis >10 mm = enlarged)
 - Stations: Paratracheal, prevascular, subcarinal, hilar
 - Mass lesions
- 3. Pleura:**
 - Effusion: Small (<500 mL), moderate (500-1000 mL), large (>1000 mL)
 - Thickening
 - Masses
- 4. Heart and great vessels:**
 - Cardiomegaly
 - Pericardial effusion
 - Vascular abnormalities

CT Abdomen/Pelvis protocol:

Scanning parameters:

- Patient position: Supine, arms above head
- Scan range: Diaphragm through symphysis pubis
- Slice thickness: [SPECIFY: e.g., "3-5 mm"]
- kVp: [SPECIFY: e.g., "120 kVp"]
- mAs: Adjusted based on patient size
- Pitch: [SPECIFY: e.g., "1.0-1.5"]

Imaging protocol:

- Non-contrast scan (optional, if evaluating for stones or calcifications)
- Portal venous phase (60-70 seconds): Standard for most abdominal evaluations
- Delayed phase (3-5 minutes): If evaluating urinary tract or masses

Image interpretation - Abdomen:

1. **Liver:**
 - Size: Measured craniocaudally in midclavicular line
 - Attenuation: Compared to spleen (normal liver slightly higher than spleen)
 - Focal lesions: Size, number, enhancement pattern
 - Morphology: Surface contour, lobar atrophy/hypertrophy
2. **Spleen:**
 - Size: Craniocaudal dimension >13 cm = splenomegaly
 - Focal lesions: Size, number, enhancement pattern
3. **Kidneys:**
 - Size: >12 cm = enlarged
 - Enhancement: Corticomedullary differentiation
 - Hydronephrosis: Graded as mild, moderate, severe
 - Focal lesions
 - Stones
4. **Lymph nodes:**
 - Location: Porta hepatis, celiac axis, para-aortic, retrocrural, mesenteric, pelvic
 - Size: Short axis >10 mm = pathologically enlarged
 - Number: Single vs. multiple station involvement
 - Enhancement pattern
5. **Gastrointestinal tract:**
 - Wall thickening: >5 mm (small bowel), >10 mm (colon)
 - Enhancement pattern
 - Masses
6. **Peritoneum:**
 - Ascites: Trace, small, moderate, large
 - Peritoneal thickening or masses
7. **Pancreas:**
 - Size, contour, attenuation
 - Focal lesions
8. **Other:**
 - Adrenal glands: Size, masses
 - Retroperitoneum: Masses, fluid collections
 - Bones: Lytic or sclerotic lesions

- Soft tissues: Masses, fluid collections

Radiation dose monitoring:

- Dose Length Product (DLP) and CT Dose Index (CTDIvol) recorded for all examinations
- Dose optimization protocols followed
- Radiation dose kept as low as reasonably achievable (ALARA principle)

Image reporting:

All CT examinations were interpreted by board-certified radiologists [SPECIFY: with relevant experience]. Reports were generated using standardized templates based on the indication for imaging. For the purposes of this study, the following specific findings were systematically extracted from radiology reports:

- Hepatomegaly (yes/no, size in cm)
- Abnormal liver attenuation (yes/no, description)
- Splenomegaly (yes/no, size in cm)
- Kidney enlargement (yes/no, size in cm)
- Hydronephrosis (yes/no, grade)
- Lymphadenopathy (yes/no, locations, largest node size)
- Pleural effusion (yes/no, side, volume estimate)
- Mediastinal lymphadenopathy (yes/no, stations involved, largest node size)
- Pulmonary nodules (yes/no, number, largest size, characteristics)
- Other relevant findings

Imaging safety:

- All imaging performed following institutional safety protocols
- Contrast allergy screening performed prior to IV contrast administration
- Premedication protocols available for patients with prior contrast reactions
- Emergency equipment and medications available in imaging suites
- All female participants of childbearing age underwent pregnancy testing before CT
- Radiation exposure minimized using appropriate protocols and dose reduction techniques

Blinding:

[SPECIFY: e.g., "Radiologists were blinded to clinical outcomes (mortality status) at the time of interpretation" OR "Radiologists were not blinded to clinical information as this was part of routine clinical care"]

Supplementary methods S4: Detailed composite score methodology

Overview

Three composite scoring systems were developed to provide comprehensive assessment of disease severity across nutritional, hematological, and radiological domains. Each composite score sums binary indicators (present/absent) of abnormalities based on established clinical thresholds. **These composite scores are novel, have not been externally validated, and were developed as exploratory tools for risk stratification in this cohort.** The rationale for developing these scores was to create simple, clinically applicable tools that integrate multiple markers of disease severity while maintaining ease of calculation at the bedside or in resource-limited settings.

1. Prognostic nutritional index (PNI)

Background:

The Prognostic Nutritional Index was originally developed by Onodera et al. in 1984 as a perioperative risk assessment tool for gastrointestinal surgery patients. The index combines serum albumin (marker of protein nutritional status and systemic inflammation) with total lymphocyte count (marker of immunonutritional status). While originally developed for surgical patients, PNI has subsequently been validated in multiple clinical contexts including cancer, cardiovascular disease, and chronic infections including HIV.

Formula:

$$\text{PNI} = [10 \times \text{serum albumin (g/dL)}] + [0.005 \times \text{total lymphocyte count (cells/}\mu\text{L)}]$$

Example calculation:

- Serum albumin = 3.2 g/dL
- Total lymphocyte count = 800 cells/ μ L
- $\text{PNI} = (10 \times 3.2) + (0.005 \times 800) = 32 + 4 = 36$

Categorization approaches:

We employed two categorization methods for PNI:

Approach 1: Established clinical cutoffs (for descriptive analysis)

Based on published literature in surgical and oncological populations:

- **Severe malnutrition:** $\text{PNI} < 35$
- **Moderate malnutrition:** $\text{PNI } 35\text{--}39.9$
- **Mild malnutrition:** $\text{PNI } 40\text{--}44.9$
- **Normal nutritional status:** $\text{PNI} \geq 45$

Rationale: These cutoffs have been used in prior studies and provide clinically meaningful categories.

Limitations: These cutoffs were not specifically validated in HIV populations and may not optimally discriminate risk in this context.

Approach 2: Cohort median (for binary classification in composite scores)

- **Low PNI:** PNI <43.5 (below cohort median)
- **Normal PNI:** PNI $\geq$ 43.5 (at or above cohort median)

Rationale: Using the cohort median ensures balanced group sizes for statistical comparisons and may better reflect the distribution of nutritional status in our specific population (treatment-naïve patients with advanced HIV disease).

Limitations: This approach is data-driven rather than based on established clinical thresholds and may not generalize to other populations.

Primary references for PNI:

- Onodera T, Goseki N, Kosaki G. Prognostic nutritional index in gastrointestinal surgery of malnourished cancer patients. *Nihon Geka Gakkai Zasshi*. 1984;85(9):1001-5. [Japanese]
- Buzby GP, Mullen JL, Matthews DC, Hobbs CL, Rosato EF. Prognostic nutritional index in gastrointestinal surgery. *Am J Surg*. 1980;139(1):160-7.

Validation in HIV populations:

- [ADD RELEVANT REFERENCES IF AVAILABLE - search PubMed for "prognostic nutritional index HIV" or similar]

2. Nutritional abnormalities composite score

Development rationale:

Malnutrition in HIV is multifactorial, involving inadequate caloric intake, malabsorption, increased metabolic demands, and chronic inflammation. Single markers (e.g., BMI alone) may not capture the full spectrum of nutritional compromise. We therefore developed a multidimensional composite score integrating anthropometric, biochemical, and calculated indices to provide comprehensive nutritional assessment.

Score components:

Each of the following abnormalities contributes 1 point (present = 1, absent = 0):

Component	Definition	Rationale/Reference
1. Low BMI	BMI <18.5 kg/m ²	WHO cutoff for adult underweight/undernutrition. Strong predictor of mortality in HIV populations.
2. Hypoalbuminemia	Serum albumin <3.5 g/dL	Established threshold for hypoalbuminemia. Reflects both protein malnutrition and systemic inflammation. Associated with increased mortality in HIV.
3. Low MUAC	MUAC <23 cm	Adult malnutrition screening threshold. MUAC reflects both muscle mass and fat stores and is easier to measure than BMI in resource-limited settings.
4. Low PNI	PNI <43.5	Below cohort median. Combines albumin and lymphocyte count.

Score calculation:

Total score = (BMI <18.5) + (Albumin <3.5) + (MUAC <23) + (PNI <43.5)

Range: 0-4 points

Example:

- Patient A: BMI 17 kg/m² (1 point), albumin 3.8 g/dL (0 points), MUAC 21 cm (1 point), PNI 38 (1 point)
- **Total score = 3 points (severe malnutrition)**

Categorical classification:

- **Score 0:** No malnutrition
- **Score 1:** Mild malnutrition
- **Score 2:** Moderate malnutrition
- **Score ≥3:** Severe malnutrition

Rationale for categories:

- Increasing scores reflect greater number of abnormal nutritional markers
- Score ≥3 (majority of markers abnormal) designated as severe to identify highest-risk patients
- Linear increase in mortality risk hypothesized with increasing score

Component relationships:

While the four components measure overlapping aspects of nutritional status, they are not completely redundant:

- **BMI** primarily reflects energy balance (calories in vs. out)
- **Albumin** reflects both protein nutrition and inflammation
- **MUAC** reflects both muscle mass and subcutaneous fat
- **PNI** combines albumin with immune status (lymphocytes)

Correlation analysis (Supplementary Table SX) shows moderate correlations between components ($r = 0.3-0.6$), suggesting they provide complementary rather than identical information.

Validation status:

This composite score is **novel and unvalidated**. While each individual component has established validity as a nutritional marker, the specific combination and scoring system used here has not been previously published or validated in any population. This score should be considered exploratory and hypothesis-generating. External validation in independent cohorts is required before clinical application.

References for individual components:

- BMI cutoffs: WHO. Physical status: the use and interpretation of anthropometry. WHO Technical Report Series 854. Geneva: WHO; 1995.
- Albumin: [ADD standard clinical chemistry references]
- MUAC: Tang AM, et al. Use of cutoffs for mid-upper arm circumference (MUAC) as an indicator or predictor of nutritional and health-related outcomes in adolescents and adults: a systematic review. Washington, DC: FHI 360/FANTA; 2013.
- PNI: See references above

3. Hematologic abnormalities composite score

Development rationale:

Cytopenias (low blood cell counts) are common in advanced HIV disease and result from multiple mechanisms including direct HIV effects on bone marrow, opportunistic infections, medications, malnutrition, and chronic inflammation. A composite score quantifying the cumulative burden of hematologic abnormalities may better predict outcomes than any single cytopenia. This score was designed to be simple and based on readily available complete blood count data.

Score components:

Each of the following abnormalities contributes 1 point (present = 1, absent = 0):

Component	Definition	Rationale/Reference
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Component	Definition	Rationale/Reference
1. Severe anemia	Hemoglobin g/dL <10	WHO definition of moderate anemia. Changed to <10 g/dL (rather than <8 g/dL for "severe") to increase sensitivity for detecting clinically significant anemia in this population.
2. Thrombocytopenia	Platelet count <100,000/ μ L	Standard clinical threshold. Mild thrombocytopenia; increases bleeding risk particularly with invasive procedures.
3. Leukopenia	Total WBC <3,000/ μ L	Clinical threshold for leukopenia. Increases infection risk.
4. Neutropenia	Absolute neutrophil count <1,500/ μ L	Clinical threshold for mild neutropenia. Increases bacterial infection risk.

Score calculation:

Total Score = (Hb <10) + (Platelets <100k) + (WBC <3k) + (ANC <1.5k)

Range: 0-4 points

Example:

- Patient B: Hb 9.2 g/dL (1 point), platelets 85,000/ μ L (1 point), WBC 5,200/ μ L (0 points), ANC 2,800/ μ L (0 points)
- **Total score = 2 points (moderate hematologic abnormalities)**

Categorical classification:

- **Score 0:** No hematologic abnormalities
- **Score 1:** Mild hematologic dysfunction
- **Score 2:** Moderate hematologic dysfunction
- **Score ≥ 3 :** Severe hematologic dysfunction

Rationale for categories:

- Score 0: Normal hematologic status
- Score 1-2: Isolated or dual cytopenias (relatively common in HIV)
- Score ≥ 3 : Pancytopenia or near-pancytopenia (marker of severe bone marrow compromise)

Pathophysiological basis:

Hematologic abnormalities in HIV result from:

- **Direct HIV effects:** HIV infection of hematopoietic progenitor cells and stromal cells in bone marrow
- **Immune-mediated destruction:** Antibodies against blood cells
- **Opportunistic infections:** Mycobacterium avium complex, cytomegalovirus, parvovirus B19, histoplasmosis can suppress bone marrow
- **Medications:** Zidovudine (anemia), ganciclovir (neutropenia), trimethoprim-sulfamethoxazole (all lineages)
- **Nutritional deficiencies:** Vitamin B12, folate, iron deficiency
- **Chronic inflammation:** Anemia of chronic disease

- **Hypersplenism:** If portal hypertension present

The composite score captures the cumulative impact of these mechanisms.

Component relationships:

The four cytopenias may co-occur (pancytopenia indicating severe bone marrow suppression) or occur independently (isolated anemia or neutropenia). Our data show [ADD from your correlation analysis] that correlations between cytopenias are weak to moderate ($r = 0.2-0.4$), supporting their inclusion as separate components.

Validation status:

This composite score is **novel and unvalidated**. While the individual thresholds for cytopenias are well-established clinically, the specific combination and scoring approach used here has not been previously published. This should be considered an exploratory tool requiring external validation.

Alternative approaches:

Other potential hematologic scoring approaches could include:

- Using more stringent thresholds (e.g., severe anemia <8 g/dL instead of <10 g/dL)
- Weighting different cytopenias differently (e.g., severe anemia might contribute 2 points)
- Including red cell distribution width (RDW) as a marker of inflammation
- Including mean corpuscular volume (MCV) to capture specific nutritional deficiencies

Our approach prioritized simplicity and use of standard clinical thresholds.

References:

- Hematologic complications of HIV: [ADD appropriate review articles or primary literature]
- Standard cytopenia definitions: [ADD clinical hematology references]

4. Imaging burden score

Development rationale:

Radiological abnormalities in advanced HIV disease reflect organ damage from opportunistic infections, malignancies, immune reconstitution inflammatory syndrome, and metabolic complications. While prior studies have examined specific imaging findings (e.g., hepatomegaly, lymphadenopathy) as isolated predictors, no prior work has quantified the cumulative radiological disease burden across multiple organ systems. We hypothesized that the number of abnormal organ systems would provide an integrated measure of disease severity that could predict mortality independent of laboratory markers.

This is the most novel aspect of our study

Score components:

Each of the following abnormalities detected on baseline imaging (ultrasound and/or CT) contributes 1 point:

Component	Definition	Imaging Modality
1. Hepatomegaly	Liver span >16 cm (US) OR enlarged liver on CT	US or CT
2. Abnormal echogenicity/attenuation	liver Bright echogenicity, fibrofatty changes (US) OR low attenuation (CT)	US or CT
3. Splenomegaly	Spleen >13 cm longitudinal dimension	US or CT
4. Kidney abnormalities	Enlarged kidneys (>12 cm) OR hydronephrosis of any grade	US or CT
5. Abdominal lymphadenopathy	Any lymph node >10 mm short axis in porta hepatis, para-aortic, mesenteric, or retroperitoneal regions	US or CT
6. Pleural effusion	Any volume of pleural fluid	CT chest
7. Mediastinal/hilar lymphadenopathy	Any lymph node >10 mm short axis in mediastinal or hilar stations	CT chest
8. Pulmonary nodules	Any nodular lesion in lung parenchyma	CT chest

Score calculation:

Total Score = Sum of abnormalities present

Range: 0-8 points

Note: A patient could theoretically have a score of 0-8, but the maximum possible score depends on which imaging studies were performed:

- If only ultrasound performed: Maximum score = 5 (components 1-5)
- If ultrasound + chest CT: Maximum score = 8 (all components)
- If ultrasound + abdominal CT only: Maximum score = 5 (but CT may detect findings missed on US)

Categorical classification:

- **Score 0:** No radiological abnormalities (imaging entirely normal)
- **Score 1:** Single organ system involvement
- **Score 2:** Two organ systems involved
- **Score ≥ 3 :** Multiple organ systems (≥ 3) involved

Rationale for categories:

- Score 0: Absence of detectable organ damage
- Score 1-2: Limited organ involvement (potentially reversible, less severe)
- Score ≥ 3 : Multisystem involvement suggesting advanced disease, higher mortality risk

The cutoff of ≥ 3 was selected based on distribution in our cohort (approximately 28% had score ≥ 3) and to identify patients with truly multisystem involvement.

Pathophysiological interpretation:

The imaging burden score may reflect:

1. **Direct HIV-related pathology:**
 - Lymphoid hyperplasia (lymphadenopathy)
 - HIV-associated nephropathy (enlarged kidneys)
2. **Opportunistic infections:**
 - Mycobacterium tuberculosis (lymphadenopathy, lung nodules, pleural effusion, hepatosplenomegaly)
 - Mycobacterium avium complex (hepatosplenomegaly, lymphadenopathy)
 - Cytomegalovirus (colitis, hepatitis)
 - Cryptococcus (lung nodules)
 - Pneumocystis jirovecii (lung findings)
 - Toxoplasma (brain lesions if CNS imaging performed)
3. **Malignancies:**
 - Kaposi sarcoma (lymphadenopathy, lung nodules, pleural effusion)
 - Non-Hodgkin lymphoma (lymphadenopathy, organomegaly, masses)
4. **Metabolic complications:**
 - Hepatic steatosis (abnormal liver echogenicity/attenuation)
 - Immune reconstitution inflammatory syndrome (IRIS) if imaging performed after ART initiation
5. **Portal hypertension/cirrhosis:**
 - Splenomegaly
 - Ascites (if present, would be noted separately)

Higher imaging burden scores likely indicate greater cumulative organ damage, which may not be fully reversible with ART and may predispose to higher mortality.

Scoring rules and adjudication:

- **Liver:** Hepatomegaly and abnormal echogenicity are scored separately (both can be present). Maximum 2 points for liver.
- **Bilateral findings:** Bilateral pleural effusions count as 1 point (not 2). Bilateral kidney abnormalities count as 1 point (not 2). We score organ systems, not individual organs.
- **Multiple nodules:** Multiple pulmonary nodules still count as 1 point total for component 8.
- **Incidental findings:** Minor incidental findings not clearly related to HIV (e.g., simple renal cysts, small hemangiomas) were not counted.
- **Unclear findings:** If a finding was noted as "borderline" or "equivocal" in the radiology report, it was reviewed by the study team and counted as present if the abnormality met the specified threshold.

Supplementary Table 1. Imaging modalities.

Imaging Parameter	Total (N=50)	Survivors (N=38)	Deaths (N=12)	P-value
Liver Size				<0.001
- Enlarged	16 (32.0%)	5 (13.2%)	11 (91.7%)	
- Normal	34 (68.0%)	33 (86.8%)	1 (8.3%)	
Liver Echogenicity				0.007
- Bright echogenicity	4 (8.2%)	4 (10.8%)	0 (0.0%)	
- Fibrofatty changes	14 (28.6%)	6 (16.2%)	8 (66.7%)	
- Normal	31 (63.3%)	27 (73.0%)	4 (33.3%)	
Spleen Size				0.105
- Enlarged	11 (22.0%)	6 (15.8%)	5 (41.7%)	
- Normal	39 (78.0%)	32 (84.2%)	7 (58.3%)	
Kidney Findings				0.003
- Enlarged	3 (6.3%)	0 (0.0%)	3 (25.0%)	
- Hydronephrosis	1 (2.1%)	0 (0.0%)	1 (8.3%)	
- Normal	44 (91.7%)	36 (100.0%)	8 (66.7%)	
Lymphadenopathy				0.141
- Absent	44 (88.0%)	35 (92.1%)	9 (75.0%)	
- Present	6 (12.0%)	3 (7.9%)	3 (25.0%)	
CT Pleural Effusion				0.426
- Absent	48 (96.0%)	37 (97.4%)	11 (91.7%)	
- Present	2 (4.0%)	1 (2.6%)	1 (8.3%)	
CT Mediastinal Lymph Nodes				0.582
- Absent	45 (90.0%)	35 (92.1%)	10 (83.3%)	
- Present	5 (10.0%)	3 (7.9%)	2 (16.7%)	
CT Lung Nodules				>0.99
- Absent	39 (78.0%)	30 (78.9%)	9 (75.0%)	
- Present	11 (22.0%)	8 (21.1%)	3 (25.0%)	
Any Liver Abnormality				<0.001
- Absent	28 (56.0%)	27 (71.1%)	1 (8.3%)	
- Present	22 (44.0%)	11 (28.9%)	11 (91.7%)	

Any Abdominal Abnormality				0.002
- Absent	26 (52.0%)	25 (65.8%)	1 (8.3%)	
- Present	24 (48.0%)	13 (34.2%)	11 (91.7%)	
Any Chest Abnormality				0.471
- Absent	35 (70.0%)	28 (73.7%)	7 (58.3%)	
- Present	15 (30.0%)	10 (26.3%)	5 (41.7%)	
Overall Imaging Status				0.018
- Any abnormality	31 (62.0%)	20 (52.6%)	11 (91.7%)	
- Normal imaging	19 (38.0%)	18 (47.4%)	1 (8.3%)	
Imaging Burden				0.001
- No abnormalities	19 (38.0%)	18 (47.4%)	1 (8.3%)	
- Single abnormality	13 (26.0%)	12 (31.6%)	1 (8.3%)	
- Two abnormalities	4 (8.0%)	2 (5.3%)	2 (16.7%)	
- Multiple abnormalities (≥ 3)	14 (28.0%)	6 (15.8%)	8 (66.7%)	
Imaging Abnormality Count	1.0 [0.0-3.0]	1.0 [0.0-1.0]	3.5 [2.0-4.0]	<0.001