

High Prevalence of Late-Stage Disease in Newly Diagnosed Human Immunodeficiency Virus Patients in Sierra Leone

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A high prevalence of late-stage disease (75.4%) and severe immunosuppression (23.3%) was observed in 155 newly diagnosed human immunodeficiency virus patients in Freetown, Sierra Leone during August to November 2017. Within the late-stage diagnosis group, a significantly high proportion of patients reported fever (84.2% vs 65.2%; $P = .01$), weight loss (82.2% vs 63.5%; $P = .01$), and malaise (89.7% vs 71.7%; $P = .05$). Fever was identified as the only independent predictor of late-stage disease in this study.

Keywords. HIV; late diagnosis; resource-limited settings; Sierra Leone.

Late-stage human immunodeficiency virus (HIV) diagnosis, defined as CD4 count <350 cells/ μ L cells and/or the presence of an acquired immune deficiency syndrome (AIDS) defining illness (ADI) at diagnosis [1] continues to present a major obstacle to efforts seeking to control the global HIV epidemic. Delayed HIV diagnosis has been associated with a higher incidence of adverse clinical events and complications [2], early mortality [3], and inflation of treatment-related costs [4]. Furthermore, it is considered a key driver of HIV transmission in the general population by HIV-infected people who are unaware of their status.

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Recent studies from East and Southern African countries have revealed that despite the expansion of HIV services across the region in recent years, late-stage diagnosis remains commonplace, ranging from 33.6% to 65.5% of newly diagnosed HIV patients [5–7]. This broad range likely reflects the heterogeneity of the inherent population characteristics, sample sizes, study designs, and the CD4 cutoff used. In comparison, data regarding late-stage diagnosis in the West African sub-region where immunological status was accessed by CD4 enumeration are scarce. One study from Guinea-Bissau (2005–2013) has reported a late-stage presentation rate of 71.8% [8], whereas another study from Nigeria recorded 85.4% during the period 2005–2010 [9].

Sierra Leone is a low-income country in West Africa where the HIV epidemic has long been regarded as low prevalence and stable, with an estimated countrywide HIV seroprevalence rate of 1.5 to 1.7% [10, 11]. However, the Ebola epidemic of 2014–2016 and other recent developmental challenges have led to considerable disruptions in HIV and other healthcare services, raising concerns that the HIV epidemic may in fact be escalating in the country [12]. This study is the first to describe the clinical and immunological characteristics of newly diagnosed HIV patients in Sierra Leone—2 objective parameters that could provide critical insight into the scale and direction of the HIV epidemic in the country.

METHODS

We conducted a cross-sectional study of 155 newly diagnosed HIV adult patients aged ≥ 18 years at Connaught Hospital in Freetown—the national referral hospital and site of the largest HIV clinic in Sierra Leone—from August through November 2017. The Institutional Review Board of University Hospitals Cleveland Medical Center granted a waiver and deferred to the Sierra Leone Ethical and Scientific Research Committee, which approved the study. After obtaining patient consent, we collected their demographic, clinical, and immunological data at the time of HIV diagnosis. Human immunodeficiency virus status was determined using the fourth-generation rapid test by SD Bioline HIV-1/2 3.0 (Standard Diagnostics, Inc.). The Alere Pima Analyzer (Abbott) was used for CD4 enumeration. This is a well validated point-of-care CD4 testing platform with proven comparable performance to flow cytometry-based methods, especially in resource-limited settings [13]. The GeneXpert MTB/RIF assay (Cepheid) and sputum AFB smear with/without chest radiography was used to determine tuberculosis positive status. Late-stage disease (CD4 <350 cells/ μ L) was further stratified into AIDS (CD4 <200 cells/ μ L and/or presence of ADI

regardless of CD4 cell count) and severe immunosuppression (CD4 <100 cells/ μ L).

Statistical analysis was performed using the SPSS Version 19.0 (IBM Corp., Armonk, NY). Descriptive statistics were used to report demographic and clinical variables. Categorical variables were presented as number of cases and percentages and were compared using the χ^2 test. Continuous variables were expressed as mean \pm standard deviation and compared using the non-parametric Mann-Whitney *U* test or Student's *t* test, where appropriate. Multivariate stepwise logistic regression analysis was used to evaluate factors independently associated with late diagnosis. Only variables with $P \leq 0.1$ in the univariate analysis were included in the multivariate analysis. $P < 0.05$ was considered statistically significant.

RESULTS

Table 1 shows the baseline demographic and clinical characteristics of the study population ($n = 155$). The majority of patients

Table 1. Main Characteristics of Newly Diagnosed HIV Patients in Sierra Leone

Variables	N = 155
Gender	
Female	92 (59.4)
Male	63 (40.6)
Age (years)	35.9 \pm 10.6
Education	
Primary	33 (21.3)
Secondary	57 (36.8)
Tertiary	30 (19.4)
None	35 (22.6)
Immunological Status (cells/μL)	
Median CD4 count	279 (IQR, 29–533)
≤ 99	33 (23.2)
100–199	43 (25.8)
200–349	39 (25.2)
≥ 350	40 (25.8)
BMI (kg/m ²)	20.9 \pm 3.4
Occupation	
Trader	60 (38.7)
Unemployed	17 (11)
Student	16 (10.3)
Driver	6 (3.9)
Teacher	5 (3.2)
Clinical Symptoms	
Weight loss	95 (61.3)
Fever	80 (51.6)
Malaise	31 (20)
Cough	23 (14.8)
Diarrhea	22 (14.2)
Rash	15 (9.7)
Lymphadenopathy	14 (9)
Other (ie, night sweats, odynophagia)	<6%

Abbreviations: BMI, body mass index; HIV, human immunodeficiency virus; IQR, interquartile range.

^aData are expressed as n (%) or mean \pm standard deviation.

were female (59.4%), with a mean age of 35.9 years (range, 25.3–46.4). Most had some form of education (77.4%), half were married (49.7%), and most had an occupation, with trader and student being the most frequently reported. All participants self-identified as heterosexuals. A low rate of drug consumption was observed: 12.9% consumed alcohol, 6.5% were smokers, and 6.5% admitted to illicit drug use.

The median CD4 cell count of the study participants was 279 cells/ μ L (interquartile range [IQR], 42–533 cells/ μ L), with 74.2% meeting the criteria for late-stage diagnosis (CD4 <350 cells/ μ L). Furthermore, 49.0% had AIDS (CD4 <200 cells/ μ L and/or ADI), and 21.3% had severe immunosuppression (CD4 <100 cells/ μ L).

Acquired immune deficiency syndrome-defining illnesses were observed in 40 participants (25.8%), including 24 cases of tuberculosis (17 pulmonary, 6 lymph node, 1 disseminated), 11 cases of esophageal candidiasis, and 5 cases of Kaposi sarcoma. The most common self-reported and/or measured clinical signs or symptoms present at least within the last 30 days before HIV diagnosis were weight loss (61.3%), fever (51.6%), malaise (20.0%), cough (14.8%), and diarrhea (14.2%). Rash (9.7%) and lymphadenopathy (9.0%) were less common.

Within the late diagnosis subgroup, a significantly high proportion of patients had fever (84.2% vs 65.2%; $P = .01$), weight loss (82.2% vs 63.5%; $P = .01$), and malaise (89.7% vs 71.7%; $P = .05$). No association was observed between fever and gender (70.7% female vs 81.7% male; $P = .10$), age (36.0 \pm 10.9 vs 35.5 \pm 10.3; $P = .45$), marital status, occupation, or illicit drug use. It is interesting to note that the median CD4 count increased with the level of education—ie, none, 222 cells/ μ L (IQR, 76–368); primary, 231 cells/ μ L (IQR, 51–441); secondary, 303 cells/ μ L (IQR, 23–583); tertiary, 357 cells/ μ L (IQR, 24–690)—with a trend towards higher median CD4 counts for tertiary education compared with secondary or lower, without demonstration of statistical significance (356 \pm 65 vs 261 \pm 21 cells/ μ L; $P = .18$). In the multivariate analysis model, the variables fever, weight loss, and malaise were included. Only fever (odds ratio [OR], 2.85; 95% confidence interval [CI], 1.29–6.34; $P = .01$) was identified as an independent predictor of late-stage presentation in this study population. Similar results were found when the analysis was performed using the CD4 threshold of < 200 cells/ μ L and/or ADI (AIDS). A significantly high proportion of patients had fever (56.6% vs 33.3%, $P = .04$), weight loss (52.2.5% vs 34.6%, $P = .03$), and cough (71.4% vs 41.3%, $P = .01$). In the multivariate analysis model, fever (OR, 2.32; 95% CI, 1.15–4.67; $P = .02$) and cough (OR, 2.95; 95% CI, 1.05–8.33; $P = .04$) independently predicted AIDS.

DISCUSSION

In this cohort of newly diagnosed HIV patients in Sierra Leone, we observed a high prevalence of late-stage diagnosis (74.2%), AIDS (49.0%), and severe immunosuppression (21.3%). To

the best of our knowledge, this is the first study to describe the prevalence, clinical features, and immunological characteristics of late-stage HIV disease in Sierra Leone. As previously noted, data from the West African subregion on this important public health subject are scarce and not up to date. Hønge et al [8] and Agaba et al [9] were referenced earlier in this regard. Very recently, a large study of IeDEA and COHERE cohorts examining global trends in CD4 cell counts at the time of antiretroviral therapy (ART) initiation included data from 7 West African countries (Benin, Burkina Faso, Guinea, Guinea-Bissau, Mali, Togo, and Nigeria) but without data from Sierra Leone [14]. They estimated a median CD4 count of 186 cells/ μ L at ART initiation in these countries in 2014 [14]. Currently, there are no published data describing the median CD4 count of newly diagnosed HIV patients at ART initiation in Sierra Leone. However, assuming that estimates from the IeDEA and COHERE West African cohorts apply to Sierra Leone suggest that there is a significant time lag between HIV diagnosis, linkage to care, and ART initiation in Sierra Leone, portending poor, long-term clinical outcomes for these patients.

The prevalence of late-stage diagnosis from the East and Southern African countries previously mentioned (range, 33.6%–65.5%) [5–7] are lower than figures observed in our study and elsewhere in West Africa [8, 9]. This improvement may be due in part to the implementation of specific interventions against the HIV epidemic in East and Southern African countries that promote HIV testing and early ART initiation.

The overall prevalence of ADIs observed in our cohort was lower (25.8%) than those that have been reported in other West African countries such as Nigeria and Gabon (range, 46.6%–85%) [15, 16]. This could be explained in part by the fact that ADIs are a heterogeneous group of infectious and noninfectious entities, many of which would pose considerable diagnostic challenges in resource-limited settings such as Sierra Leone. Therefore, we presume that the actual prevalence of ADIs may in fact be much higher.

The high prevalence of fever (84.2% of late presenters, 51.6% overall) and its emergence as the sole independent predictor of late-stage HIV presentation in this study is noteworthy. Indeed, Ansumana et al [17] recently reported that 8.9% of febrile illness in a large cohort of adults and children ($n = 1207$) in Bo, Sierra Leone in 2013–2014 was due to HIV infection. Willoughby et al [18] previously reported a 92.5% occurrence of fever in 106 patients presenting with strong clinical suspicion for HIV infection in Freetown (14.9% HIV prevalence) during 1999–2000. This observation may have implications for diagnosis of febrile illnesses in Sierra Leone and sub-Saharan Africa, where the focus is usually on malaria and typhoid fever.

The limitations of our study arise mainly from the sample size, restriction to a single study location in an urban area, and selection bias due to provider-initiated testing of already very ill patients in the clinic, rather than asymptomatic and

otherwise well appearing people seeking voluntary testing. Notwithstanding, the results of this study merit attention given the lack of scientific data on this relevant public health subject in Sierra Leone.

CONCLUSIONS

In summary, a high prevalence of late-stage HIV diagnosis was reported in Sierra Leone for the first time. Fever emerged as the sole predictor of late-stage disease in this cohort. These findings underscore the urgent need to conduct larger studies to determine the scale of the problem, investigate the trends and clinical outcomes, as well as define the correlates and determinants of late-stage presentation that are undermining current national and international efforts seeking to monitor and control the HIV epidemic in Sierra Leone.

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