

# Clinical Profiles of HIV-Infected, HAART-Naive Patients Admitted to a Tertiary Level Hospital in Maseru, Lesotho

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## Abstract

**Introduction:** Southern Africa has one of the highest HIV prevalence rates globally. The HIV epidemic in the region is characterised by high rates of morbidity and mortality. The aim of this study was to document the clinical profiles of patients hospitalised for the treatment of HIV-related disorders in Maseru, Lesotho. **Methods:** A prospective observational study of 105 HIV-infected, HAART-naïve patients admitted at Queen Elizabeth II Referral Hospital in Maseru. **Results:** The median age was 34 years and 50.5% were female. 74 patients (70.5%) had tested positive for HIV before admission. 85.9% of all patients had presented with Stage III or IV events at diagnosis of HIV infection. 69.5% of the patients were treated for opportunistic infections of which tuberculosis was the commonest ( $n = 43$ , 41.0%) followed by oral candidiasis ( $n = 19$ , 18.1%) and pneumonia ( $n = 11$ , 10.5%). 35 patients (33.3%) had severe anaemia ( $Hb < 8g/dl$ ). The median CD4 count was 73.5 cells/ $\mu l$ ; 62 patients (59.0%) were in Stage III and 43 (41.0%) were in Stage IV of HIV infection. The median duration of hospitalisation was 9 days; prolonged hospitalisation was associated with extrapulmonary tuberculosis and cryptococcal meningitis. The in-hospital mortality was 30.5%; the mortality rate was higher among patients with advanced AIDS (Stage IV). **Conclusions:** The majority of the patients presented with HIV-related opportunistic infections. The main factors contributing to morbidity and mortality in this study were late presentation for diagnosis of HIV infection and treatment of HIV-related disorders.

## INTRODUCTION

Southern Africa has one of the highest HIV prevalence rates globally. Lesotho is among the worst affected countries by HIV/AIDS in the region. At the end of 2004, the national HIV prevalence for persons aged 15 to 49 years was estimated at 23.2% [1]. Most people living with HIV/AIDS are women (56% of the adults); and prevalence rates of more than 80% have been reported among people with tuberculosis [1, 2].

It is well established that early initiation of anti-retroviral therapy (ART) can reduce both morbidity and mortality in HIV-infected patients [3-5]. Since 2004, efforts have been made to scale up ART delivery to all HIV-infected persons who qualify for ART in Lesotho. In spite of these measures, the HIV epidemic in Lesotho is still characterised by a high case-fatality ratio. In 2007/8, HIV/AIDS accounted for 10% and 12% of all adult male and female admissions to public sector hospitals in Lesotho and, over the same period, for 26% and 31% of male and female institutional deaths respectively [6].

The clinical features of HIV-infected patients at HIV

diagnosis in Lesotho and the factors associated with hospitalisation in HIV-infected persons have not been studied. The aim of this study was to report the clinical and laboratory profiles of HIV-infected, ART-naïve patients hospitalised for the management of HIV-related disorders in Maseru, Lesotho.

## METHODS

A prospective observational study was conducted at Queen Elizabeth II (QE II) Referral Hospital in Maseru, Lesotho. QEII Hospital is a public sector tertiary level hospital; it is also the national referral hospital. The study population included consecutive 105 adult patients ( $> 15$  years) admitted to the male and female wards between July and October 2010. Patients were included if they were HIV seropositive (either known to be seropositive prior to admission or tested positive following admission), not receiving highly active anti-retroviral therapy (HAART) and admitted for the treatment of HIV-related disorders.

All patients gave informed consent for taking part in the study. Patient demographic information, medical history including diagnosis of HIV-infection, diagnosis and

treatment of opportunistic infections and other HIV-related disorders were obtained from the patient medical records using predesigned data collection forms. All patients were clinically evaluated for the following AIDS-defining illnesses: tuberculosis, *Pneumocystis jiroveci* pneumonia, extrapulmonary cryptococcosis, candidiasis and wasting. Clinical staging of patients was based on the World Health Organisation (WHO) criteria for the Clinical Staging of Established HIV Infection [7]. Investigations included full blood count, liver function tests and urea and electrolytes, blood culture and CD4 count. Clinical care was provided by the institutional staff according to hospital protocols.

The study protocol was approved by the Lesotho Ministry of Health & Social Welfare (MOHSW) Ethics Committee.

Data was analysed using EpiInfo Version 3.5.3.

Demographic variables and laboratory parameters are presented as median with interquartile range and the frequency of various symptoms and signs and opportunistic infections as percentages. Comparisons between data (where indicated) were done using a Student's t-test. A p-value of < 0.05 was considered significant.

## RESULTS

A total of 130 HIV-infected, HAART-naïve patients were enrolled in the study; 25 patients were excluded due to incomplete laboratory data leaving 105 patients for analysis. Table 1 shows the demographic characteristics and medical history of the study population. 50.5% of the patients were female, the median age was 34 (range, 16 – 88) years) and more than 80% of the patients were aged ≤ 49 years. Of the 74 patients who had tested positive for HIV prior to admission, 19 (25.7%) were diagnosed within the 3 months, 47 (63.5%) between 3 months and 1 year and 8 (10.8%) more than 1 year before the current hospitalisation. 15 patients (14.3%) had a history of antituberculosis treatment (ATT), 17 (16.2%) were receiving ATT and 23 (21.9%) were using cotrimoxazole.

**Figure 1**

Table 1. Demographic characteristics and medical history of the study population

	Number of patients (%)
<b>Gender</b>	
Male	52 (49.5)
Female	53 (50.5)
<b>Age in years</b>	
Median age (IQR)	34 (29 - 44)
≤ 49	90 (85.7)
> 49	15 (14.3)
<b>HIV status on admission</b>	
Positive	74 (70.5)
Unknown	31 (29.5)
<b>Previous ATT</b>	15 (14.3)
<b>Concomitant drug intake</b>	
ATT	17 (16.2)
Cotrimoxazole	23 (21.9)
<b>Symptoms/Signs</b>	
<b>Respiratory System</b>	
Cough	48 (45.7%)
Dyspnoea	15 (14.3%)
Night sweats	16 (15.2%)
<b>Central Nervous System</b>	
Confusion	17 (16.2%)
Headache	17 (16.2%)
Neck stiffness	15 (14.3%)
<b>Gastrointestinal System</b>	
Diarrhoea	17 (16.2%)
Vomiting	15 (14.3%)
Generalised weakness*	35 (33.3%)
Weight loss/wasting**	35 (33.3%)

\*Generalised body weakness manifested as the inability to walk; \*\*weight loss reported by the patient and/or wasting evaluated clinically by the attending physician.

The most common symptom was cough (n = 48, 45.7%) followed by weight loss/wasting and generalised weakness (n = 35, 33.3%). The median time interval between onset of symptoms and hospital admission was shortest for headache (7 days) and longest for cough and diarrhoea (> 1 month).

Table 2 summarises the baseline laboratory data of the patients. 76 patients had anaemia (defined as Hb < 11.1 g/dL; nearly half of these (n = 35) had severe anaemia (Hb < 8 g/dL). The prevalence of anaemia was higher among females than males at 84.9% and 59.6% of all female and male patients respectively. The mean haemoglobin level was lower for females; (mean ± SD) 8.5 ± 2.7 g/dL vs. 10.0 ± 3.2 g/dL for males, p = 0.01. 20 patients had thrombocytopenia (platelet counts < 100 x 10<sup>3</sup>/μl) though only one patient presented with severe bleeding disorders. Elevated liver enzymes (ALT > 2.5 x Upper Limit of Normal) were found in 13 patients (12.4%). CD4 cell counts were available for 76 patients. 57 patients had CD4 cell counts < 200 cells/μl; among these 28 patients (36.8%) had CD4 counts < 50

cells/ $\mu$ l.

**Figure 2**

Table 2. Laboratory data of 105 HIV-infected, HAART-naïve patients

Laboratory Parameter	Median (IQR)	Range	Reference Values
RBC ( $\times 10^6/\mu$ l)	3.2 (2.6 – 3.8)	0.65 – 6.42	4.50 – 6.50
Hb (g/dl)	9.2 (7.2 – 11.4)	2.3 – 18.3	13.0 – 17.0
HCT (%)	27.2 (21.8 – 32.6)	6.3 – 57.8	40.0 – 54.0
PLT ( $\times 10^3/\mu$ l)	34.0	2 – 687	150 – 500
ALT (mmol/l)	208 (119 – 285)	5 – 365	0 – 40
AST (mmol/l)	36 (20 – 67)	12 – 807	0 – 37
Urea ( $\mu$ mol/l)	76 (42 – 134)	2.1 – 428	1.7 – 8.3
Creatinine ( $\mu$ mol/l)	8.15 (5.4 – 16.4)	24.2 – 1393	44 – 97
CD4 counts (cells/ $\mu$ l)	101 (72 – 168)	1 – 674	
(n = 76)	73.5 (27 – 194)		
	$\geq 350$ n = 12		
	200 – 349 n = 7		
	< 200 n = 57		

73 patients (69.5%) were treated for opportunistic infections (OI), Table 3. The commonest OI was tuberculosis (n = 43, 41.0%) followed by oral candidiasis (n = 19, 18.1%) and pneumonia (n = 11, 10.5%). 39 of the 43 TB patients (90.7%) had pulmonary tuberculosis. The most common non-infectious HIV-related disease was anaemia (n = 76, 72.4%). 5 patients were diagnosed with symptomatic HIV-associated nephropathy and 1 patient with Kaposi Sarcoma. The clinical staging of patients was carried out using the WHO guidelines for the Clinical Staging of HIV/AIDS for adults; 62 patients (59.0%) were in Stage 3 and 43 (41.0%) were in Stage 4 of HIV infection.

**Figure 3**

Table 3. Opportunistic infections and non-infectious HIV-related diseases among the study population

Diagnosis	Frequency, n (%)
Tuberculosis	43 (41.0%)
PTB	39
ePTB*	4
Oral candidiasis	19 (18.1%)
Pneumonia	11 (10.5%)
Bacterial meningitis	6 (5.7%)
Cryptococcal meningitis	4 (3.8%)
Oesophageal candidiasis	4 (3.8%)
Fungal skin and/or nail infections	2 (1.9%)
Anaemia	76 (72.4%)
HIV-associated nephropathy	5 (4.8%)
Kaposi Sarcoma	1 (1.0%)
Clinical Staging of Patients	
Stage 3	62 (59.0%)
Stage 4	43 (41.0%)

\*ePTB: extrapulmonary tuberculosis

76 patients (72.4%) were started on empiric antibiotic therapy following admission. Of these 73 (96.1%) were diagnosed as having infectious HIV-related disorders and initiated on appropriate antibiotic and/or antifungal treatment according to hospital protocols. ATT was started in 26 newly diagnosed TB patients; patients with cryptococcal meningitis were started on a 14-day course of amphotericin B. The median duration of hospitalisation was 9 (IQR, 6 – 15) days, Table 4. Prolonged hospitalisation was associated with extrapulmonary TB (median 16.5, IQR 16 – 17 days) and cryptococcal meningitis (median 16.5, IQR 14 – 19 days) infection. Of the 32 patients who died during hospitalisation, 20 had HIV-related opportunistic infections and 12 other manifestations of advanced HIV infection including HIV wasting syndrome, neurological symptoms and hepatorenal insufficiency. In general the mortality rate was higher among patients in clinical stage 4 (n = 18/43 patients, 41.9%) than patients in stage 3 of HIV infection (n = 14/62 patients, 22.6%).

**Figure 4**

Table 4. Duration of hospitalisation and treatment outcomes in patients with opportunistic infections

Diagnosis	Number of patients	In-hospital stay median (IQR)	Mortality (n, %)
	105	9 (6 – 15)	32 (30.5)
Pulmonary tuberculosis	39	11 (7 – 14)	11 (10.5)
Pneumonia	11	9 (4 – 12)	3 (2.9)
Bacterial meningitis	6	8 (7 – 14)	4 (3.8)
Cryptococcal meningitis	4	16.5 (14 – 19)	2 (1.9)
Extrapulmonary TB	4	16.5 (16 – 17)	0 (0.0)

## DISCUSSION

We studied the demographic variables, clinical features and laboratory profiles of 105 HIV-infected, HAART-naive patients admitted to a tertiary level hospital in Lesotho and identified factors associated with in-hospital mortality among this study population. We found an equal distribution of males to females among patients admitted for treatment of HIV-related disorders over the study period; the median age was 34 years with more than 90% of the patients aged  $\leq 49$  years. There was an almost equal proportion of males to females among the 25 – 34, 35 – 49 and  $> 49$  years age groups; the exception was the 15 – 24 age group in which 83.3% of the patients (10 out of 12) were female. According to the Lesotho Demographic and Health Survey (2004) [1], HIV prevalence is higher in women than in men under 30 years and the pattern reverses among people aged 40 – 49 years.

More than a third of the patients ( $n = 43$ , 41.0%) were treated for tuberculosis. Tuberculosis is the leading HIV-related opportunistic infection in developing countries; it is also one of the main causes of death among HIV-infected people [8, 9]. Timely initiation of cotrimoxazole prophylaxis, anti-tuberculosis therapy and/or antiretroviral therapy reduces mortality in HIV/TB co-infection [10 – 15]. All patients who were receiving ATT at admission ( $n = 17$ ) were using cotrimoxazole; however the majority ( $n = 15$ , 88.2%) had received treatment for less than one month. Of the 26 newly diagnosed TB patients, 18 were recently diagnosed with HIV infection ( $< 3$  months) and 8 were diagnosed following admission; 19 patients (73.1%) presented with chronic cough and 16 (61.5%) reported significant weight loss for more than one month. The median haemoglobin level was 8.6 (IQR 7 – 10) g/dL and median CD4 count 99 (IQR = 50 – 300) cells/ $\mu$ L. These findings indicate late presentation to HIV/TB care among this specific sub-population. The delay in diagnosing TB in HIV/TB co-infection is associated with risk of clinical deterioration on starting ATT [16-18].

More than two thirds of the study participants had anaemia. Anaemia is the most common haematological disorder in advanced HIV infection [19 – 22]. The levels of haemoglobin in this study are lower than those previously reported elsewhere [22]. This may be partly explained by the higher proportion of females included in this study (50.5%); iron deficiency anaemia has been reported in 43% of females aged 15 – 49 years in Lesotho [23]. We did not determine

whether the anaemia among in this study was principally due to iron deficiency or whether it was anaemia of chronic disease. In Lesotho, mild to moderate anaemia is routinely treated with micronutrient supplements. The treatment options for severe anaemia in advanced HIV infection include blood transfusions and erythropoietin therapy [24 – 26], both of which are generally not readily accessible and/or affordable to the majority of patients in resource-constrained settings.

We observed an overall mortality rate of 30.5%. The high mortality rate can be explained by the high proportion of critically ill patients that were included in the study. More than 90% ( $n = 96$ ; 91.4%) of the patients in this study were admitted via the hospital's emergency department, and only 9 (8.6%) had been referred from primary health care/first level referral centres. This further supports our observation of delayed treatment-seeking for HIV-related disorders among the study population. A retrospective analysis of outpatient medical records showed that 79.7% (59/74) of the patients known to be seropositive for HIV infection prior to admission had presented with Stage 3 or 4 events at diagnosis. Late testing for HIV infection and delayed presentation to HIV care are both associated with a higher mortality in HIV-infected patients [27 – 30].

## CONCLUSIONS

Lesotho has adopted the WHO recommendations aimed at earlier diagnosis of HIV infection and ART initiation. In addition, pre-ART services, cotrimoxazole preventive therapy and ARV drugs are provided free of charge in the public sector. Our results show that the main contributing factors to morbidity and mortality among the study population were late presentation at diagnosis of HIV infection and delayed treatment seeking for HIV-related disorders. Both health care system resource constraints and patient-mediated factors may lead to late diagnosis of HIV infection. Further studies are required to assess the extent of this problem and to identify the factors leading to late presentation in HIV infection in Lesotho.

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