OUTCOMES AND SIDE EFFECTS OF PATIENTS ON ART FOR MORE THAN 10 YEARS IN MALAWI

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Background

- With the support of MSF, antiretroviral drugs (ART) have been available in Chiradzulu district, Malawi, since 2001.
- We conducted a cross-sectional study among individuals on ART for more than 10 years to assess long term clinical, immunological, virological outcomes and prevalence of major side effects.

Objectives

- To describe clinical, immunological, and virological outcomes of patients on long term ART
- To describe the characteristics of patients on long term ART

Methods

Study design and study population

- A cross-sectional study conducted during the period November 2015 to June 2016.
- Patients, on ART for >10 years identified using the routine electronic HIV cohort monitoring database (FUCHIA)

Inclusion criteria :

- Age ≥ 30 years,
- initiated ART in Chiradzulu,
- on ART for ≥ 10 years .

Ethics:

- Each patient provided signed informed consent before participation
- Study approved by the National Research Committee of Malawi.

Study procedures

- Individual patient ART history collected from Fuchia database
- Clinical Research Forms collected demographic, medical background information as well as clinical and laboratory data.
- The ACTG Brief Peripheral Neuropathy Screening Tool used to assess Peripheral Neuropathy ; defined as subjective neuropathy >zero and at least one bilateral objective finding.
- Facial atrophy measured subjectively through observation by the clinical officer and patient verification
- Blood collected for CD4 (Cyflow SL, Partec, Munster, Germany) and Viral load (Samba, Diagnostics for the Real World, Sunnyvale, USA)

Analysis

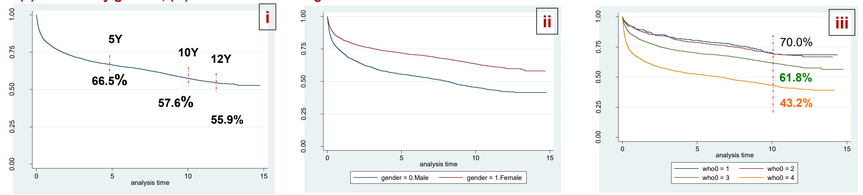
- Kaplan-Meier estimates was used to estimate the retention in care stratified by gender and WHO stage

Results

A/ Chiradzulu Cohort Description

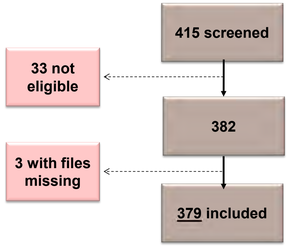
- 6572 patients initiated ART from February 2001 to February 2006
- Female; 66%, median age at ART initiation; 35.3 years [IQR 30.0 - 42.7]
- Most initiate with advanced HIV; WHO stage IV: 26.5% in female and 37.1% in males (11.8% missing WHO stage at initiation)
- At end of follow-up, 19.4% died, 21.1% LTFU, 13.6% transferred, 45.7% alive on follow up
- Retention in care at 10 years for patients initiated ART 2001-2006 was 57.6% (95%CO 56.3-58.8); higher in female vs males (63.5% vs 45.6%; Logrank p <0.01); and higher in those with initial WHO stage 1 and 2 vs those with WHO stage 3 or 4 (Logrank p <0.01)

Figure 1: Kaplan-Meier retention estimates for patients initiating ART between 2001 and 2006 in Chiradzulu Malawi: (i)Overall , (ii)stratified by gender , (iii) and initial WHO stage.



B/ Study inclusion and demographic characteristics

Figure 2: Study inclusions



- Reason for non- eligibility: less than 30 years old; 18.5% (n=6) or <10 years on ART;78.8% (n=26) at time of screening.

Table 1:Demographic characteristics

	Female n(%)	Male n(%)	Total n(%)
Age			
:30-44 yeas	120 (43.3)	19 (18.6)	139 (36.7)
45-59 years	136 (49.1)	66 (64.7)	202 (53.3)
≥60 years	21 (7.6)	17 (16.7)	38 (10.0)
Marital status:			
Never married/single	2 (0.7)	1 (0.9)	3 (0.8)
Married/ living together	115 (41.7)	89 (87.3)	204 (54.0))
Divorced/ separated	64 (23.2)	7 (6.9)	71 (18.8)
Widowed	95 (34.4)	5 (4.9)	100 (26.5)
Level of education:			
Primary education	210 (76.4)	51 (50.0)	261 (69.2)
Secondary education	65 (23.6)	51 (50.0)	116 (30.8)

C/ Medical History

- 92.1% (95%CI 88.9- 94.4) of patients ever experienced at least one WHO stage 3 or 4 event
- Median CD4 at initiation 199 cells/uL [IQR 121 - 310]
- 42.6% (95%CI 37.6 - 47.7) with history of TB
- 45% (95%CI 40 - 50) with history of severe weight loss

History of ART related toxicity

- 63.1% (95%CI 58.1 to 67.8) of patients had a severe toxicity leading to at least one drug regimen change: Lypodistrophy; 46.4% (95%CI 41.5 to 51.5) and Peripheral neuropathy ;14.0% (95%CI 10.8 to 17.9) were the most common side effects that led to drug changes whilst Lactic acidosis was less common;1.3% (95%CI 0.5 to 3.1).Other toxicities included Stephen Johnson Syndrome (n=2), Severe hepatitis, severe anaemia (n=1).

D/ Outcomes on ART > 10 years

- Median time on ART: **11.6 years** [IQR 10.6- 12.1]
- **91%** on first line regimen (86.6% on TDF based regimens)
- Most of patients 88.5% (n=324) currently asymptomatic (WHO stage 1)

CD4 and Viral Load

- Median current CD4 was 552 [IQR 410 to 700] Females had higher median CD4 counts compared to males; 572 [IQR 441 to 722] vs 485 [IQR 341 to 674]; p value= 0.014.
- Viral suppression in **92.7%** (95%CI 90.6 – 94.4)
- No gender difference in VL suppression (92.4% of female vs 91.2% male)

Figure 3: Distribution of current CD4

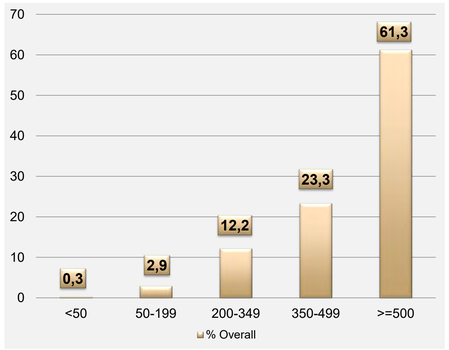


Table 2: Viral Load according to patient characteristics

Characteristic	Total (N)	Proportion with detectable viral load: n (%)
Sex:		
Female	277	21 (7.6)
Male	102	9 (8.8)
Current ART regimen:		
On 1st line regimen	321	22 (6.4)
On 2nd/3rd line	36	8 (22.2)
Current CD4:		
<200	12	6 (50.0)
≥200	365	24 (6.6)

E/ ART related side effects

- Prevalence of facial atrophy was 55.3% (95%CI: 50.2 to 60.3)
- Prevalence of peripheral neuropathy was 26.1% (95%CI :21.9 to 30.8)

Table 3: Facial atrophy and peripheral neuropathy according to different patient characteristics

Patient characteristic	Facial atrophy	χ^2 Test	Peripheral neuropathy	χ^2 Test
Sex:				
Female	52.2 (46.3- 58.1)	**0.04**	23.6 (18.9- 29.1)	0.077
Male	63.7 (54.0- 72.5)		32.7 (24.4- 42.4)	
Education level:				
Primary or less	56.6 (50.5- 62.5)	0.57	22.0 (17.3- 27.5)	**<0.01**
Secondary or more	53.5 (44.3- 62.3)		35.7 (27.4- 44.8)	
Initial ARV regimen:				
AZT	42.5% (8.3-58.1)	**0.02**	25.6 (14.4- 41.5)	0.583
D4T	57.4% (52.0-62.6)		26.4 (21.9- 31.4)	
Initial CD4 count:				
≤200	60.5 (52.5- 68.0)	0.07	26.7 (19.3- 33.2)	0.815
>200	50.0 (42.1- 57.9)		26.9 (20.3- 34.5)	

Discussion

- Good clinical and virological outcomes achieved in those retained in care
- Many patients experienced advanced HIV (WHO stages 3 and 4), and side effects leading drug regimen change.
- Lipodystrophy and peripheral neuropathy still common side-effects: perhaps due to history of prolonged use of D4T.

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