Predictors of incident hypertension in HIV-positive adults over 24 months on ART in South Africa

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BACKGROUND

As the current HIV population ages and access to antiretroviral therapy (ART) increases in resource-limited settings, the number of patients developing non-communicable chronic diseases on ART will also increase.

OBJECTIVE

In view of limited research on this topic in resource-limited settings, we sought to examine predictors of hypertension in a large urban HIV clinic in South Africa.

METHODS

- Prospective study of hypertension over 24 months on ART.
- ART naïve adults initiating ART at Themba Lethu Clinic in Johannesburg between April 2004-2011.
- Patients with hypertension at ART initiation were excluded.
- Cox regression was used to examine demographic and clinical characteristics at ART initiation in relation to incident hypertension.
- Hypertension was defined in two ways:
  1. systolic blood pressure (BP) >140 and/or diastolic BP >90 mmHg and/or documentation of hypertensive medication.
  2. categorized as mild (systolic BP 140-159.9 and/or diastolic BP 90-99.9 mmHg) or moderate/severe (systolic BP ≥160 and/or diastolic BP ≥100 mmHg).
- Person-time started at ART initiation and ended at the earliest of hypertension, loss, death, transfer or completion of 24 months of follow-up.

RESULTS

Table 1. Demographic and clinical characteristics of patients on ART, Themba Lethu Clinic, Johannesburg, South Africa (n=12 376)

Variable		Total
Gender (n, %)	female	7719 (62.4)
Age (years)	median (IQR)	36.0 (31.0-42.2)
BMI (kg/m²) (n, %)	<18	2784 (22.5)
	18-24.9	7086 (57.3)
	25-29.9	1847 (14.9)
	30-34.9	508 (4.1)
	35-39.9	111 (0.9)
	≥40	40 (0.3)
BMI (kg/m²)	median (IQR)	21.1 (18.8-24.1)
Initiating NRTI (n, %)	tenofovir	2017 (16.3)
	stavudine	4657 (37.6)
Initiating NNRTI (n, %)	efavirenz	929 (7.5)
	nevirapine	11447 (92.5)
CD4 count (cells/mm³) (n, %)	>200	1716 (13.9)
	101-200	4196 (33.9)
	51-100	2452 (19.8)
	≤50	4012 (32.4)
CD4 count (cells/mm³)	median (IQR)	94 (35-166)
WHO stage (n, %)	III/IV	5390 (43.6)
Hb (n, %)	<10 ug/dL	3239 (26.2)

MAIN FINFINGS:

- Among 17378 eligible patients, 28.8% (5002) had documented hypertension at ART initiation.
- The remaining 12 376 were predominately female (62%) and on stavudine-lamivudine-efavirenz (75%). At ART initiation patients had a median age of 36 years (IQR: 31-42), median CD4 count of 94 cells/mm³ (IQR: 35-166), median systolic blood pressure of 113 mm/Hg (IQR: 103-123) and median diastolic blood pressure of 73 mm/Hg (IQR: 66-80).

Table 2. Predictors of hypertension after 24 months on ART at Themba Lethu Clinic, Johannesburg, South Africa (n=12 376)

		Hypertension 24 Months			Mild Hypertension 24-month			Moderate/Severe Hypertension 24-month		
		Hyper-tension (n, %)	Crude HR (95% CI)	Adjusted HR (95% CI)	Hyper-tension (n, %)	Crude HR (95% CI)	Adjusted HR (95% CI)	Hyper-tension (n, %)	Crude HR (95% CI)	Adjusted HR (95% CI)
Initiating NRTI	tenofovir	288 (14.3)	1.0	1.0	263 (13.0)	1.0	1.0	21 (1.0)	1.0	1.0
	stavudine	1868 (18.0)	1.2 (1.1-1.4)	1.3 (1.1-1.4)	1594 (15.4)	1.1 (1.0-1.3)	1.2 (1.0-1.3)	2.8 (2.3)	2.1 (1.4-3.4)	2.2 (1.4-3.5)
Initiating NNRTI	efavirenz	1957 (17.1)	1.0	1.0	1686 (14.7)	1.0	1.0	232 (2.0)	1.0	1.0
	nevirapine	199 (21.4)	1.2 (1.1-1.4)	1.5 (1.3-1.7)	171 (18.4)	1.2 (1.0-1.4)	1.5 (1.3-1.8)	27 (2.9)	1.4 (1.0-2.1)	1.8 (1.2-2.6)
Age at ART initiation (yrs.)	18-24.9	50 (8.1)	0.5 (0.4-0.7)	0.6 (0.4-0.8)	40 (6.5)	0.5 (0.3-0.7)	0.5 (0.4-0.7)	9 (1.5)	0.9 (0.5-1.8)	0.9 (0.5-1.8)
	25-29.9	176 (9.1)	0.6 (0.5-0.7)	0.6 (0.5-0.7)	148 (7.7)	0.5 (0.4-0.7)	0.6 (0.5-0.7)	26 (1.4)	0.8 (0.5-1.3)	0.8 (0.5-1.3)
	30-39.9	900 (15.6)	1.0	1.0	794 (13.8)	1.0	1.0	93 (1.6)	1.0	1.0
	40-49.9	693 (15.6)	1.6 (1.4-1.7)	1.6 (1.4-1.7)	605 (20.0)	1.6 (1.4-1.7)	1.5 (1.4-1.7)	74 (2.4)	1.6 (1.2-2.2)	1.7 (1.2-2.3)
	≥50	337 (32.4)	2.5 (2.2-2.9)	2.5 (2.2-2.9)	270 (26.0)	2.3 (2.0-2.6)	2.3 (2.0-2.6)	57 (5.5)	4.2 (3.1-5.9)	4.3 (3.1-6.0)
Sex	Female	1251 (16.2)	1.0	1.0	1056 (13.7)	1.0	1.0	163 (2.1)	1.0	1.0
	Male	905 (19.4)	1.3 (1.2-1.4)	1.4 (1.2-1.5)	801 (17.2)	1.4 (1.3-1.5)	1.4 (1.3-1.6)	96 (2.1)	1.1 (0.8-1.4)	1.1 (0.9-1.5)
BMI at ART initiation (kg/m²)	<18	355 (12.8)	0.9 (0.8-1.0)	0.9 (0.8-1.0)	301 (10.8)	0.9 (0.7-1.0)	0.8 (0.7-1.0)	49 (1.8)	1.2 (0.9-1.7)	1.1 (0.8-1.5)
	18-24.9	1168 (16.5)	1.0	1.0	1020 (14.4)	1.0	1.0	129 (1.8)	1.0	1.0
	25-29.9	431 (23.3)	1.5 (1.3-1.6)	1.5 (1.3-1.7)	369 (20.0)	1.4 (1.3-1.6)	1.5 (1.3-1.7)	53 (2.9)	1.6 (1.2-2.2)	1.6 (1.2-2.3)
	30-34.9	140 (27.6)	1.7 (1.5-2.1)	1.8 (1.5-2.2)	119 (23.4)	1.7 (1.4-2.0)	1.8 (1.5-2.2)	16 (3.2)	1.8 (1.1-3.0)	1.9 (1.1-3.3)
	35-39.9	45 (40.5)	2.7 (2.0-3.7)	2.8 (2.0-3.8)	35 (31.5)	2.4 (1.7-3.4)	2.5 (1.8-3.5)	8 (7.2)	4.5 (2.2-9.2)	4.4 (2.1-9.2)
	≥40	17 (42.5)	2.8 (1.7-4.5)	2.8 (1.7-4.5)	13 (32.5)	2.4 (1.4-4.2)	2.4 (1.4-4.2)	4 (10.0)	6.0 (2.2-16.3)	6.0 (2.2-16.5)
CD4 count at ART Initiation (cells/mm³)	>200	213 (18.4)	1.0	1.0	275 (16.0)	1.0	1.0	35 (2.0)	1.0	1.0
	101-200	735 (17.5)	1.0 (0.8-1.1)	1.0 (0.8-1.1)	627 (14.9)	0.9 (0.8-1.1)	1.0 (0.8-1.1)	91 (2.1)	1.0 (0.7-1.4)	1.0 (0.7-1.5)
	51-100	445 (18.2)	1.0 (0.9-1.2)	1.0 (0.9-1.2)	274 (15.3)	1.0 (0.9-1.2)	1.0 (0.9-1.2)	64 (2.6)	1.3 (0.9-2.0)	1.3 (0.8-1.9)
	0-50	660 (16.5)	1.0 (0.9-1.2)	1.1 (1.0-1.3)	681 (14.5)	1.1 (0.9-1.2)	1.1 (1.0-1.3)	69 (1.7)	0.9 (0.6-1.4)	1.0 (0.6-1.5)
Hb at ART initiation (ug/dL)	≥10.0	1645 (18.0)	1.0	1.0	1429 (15.6)	1.0	1.0	187 (2.1)	1.0	1.0
	>10.0	511 (15.8)	1.1 (1.0-1.2)	1.2 (1.1-1.4)	428 (13.2)	1.0 (0.9-1.1)	1.2 (1.1-1.3)	72 (2.2)	1.3 (1.0-1.7)	1.5 (1.1-2.0)
WHO stage at ART initiation	I/II	1281 (18.3)	1.0	1.0	1106 (15.8)	1.0	1.0	149 (2.1)	1.0	1.0
	III/IV	875 (16.2)	1.0 (0.9-1.1)	1.0 (0.9-1.1)	751 (13.9)	0.9 (0.9-1.0)	1.0 (0.9-1.1)	110 (2.0)	1.0 (0.8-1.3)	1.1 (0.8-1.4)

MAIN FINFINGS (Cont.):

- By 24 months, 2116 (17%) developed hypertension, of whom 1857 (88%) were mild and 259 (12%) were moderate/severe.
- Regression models showed older patients (≥40 years), males, and patients with a BMI ≥25 kg/m² had an increased rate of hypertension over 24 months (Table).
- Results for mild hypertension were similar, while results for moderate/severe hypertension showed a higher hazard for patients ≥50 years and those with a BMI ≥35 kg/m².

CONCLUSIONS

20% of patients in our cohort developed hypertension within 24 months on ART. Obese patients (BMI >30kg/m2) and those older >40 years of age, should be targeted for frequent BP monitoring and identification of other cardiovascular risk factors in order to implement lifestyle modifications and pharmaceutical therapy as indicated to help prevent myocardial infarction, heart failure, stroke and kidney disease.

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