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nViremia and drug resistance among HIV-1 patients on antiretroviral treatment – a cross-sectional study in Soweto, South Africa

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Abstract

Background: We assessed risk factors for viremia and drug resistance (DR) among long-term recipients of antiretroviral therapy (ART) in South Africa.

Methods: In 2008, we conducted a cross-sectional study among patients receiving ART for ≥12 months. Genotypic resistance testing was performed on individuals with a viral load >400 RNA copies/ml. Multiple logistic regression analysis was used to assess associations.

Results: Of 998 subjects, 75% were women with a median age of 41. Most (64%) had been on treatment for >3 years. The prevalence of viremia was 14% (n=139); 12% (102/883) on first-line (i.e. NNRTI based regimen) and 33% (37/115) on second-line (i.e. PI based regimen) ART. Of viremic patients, 78% had DR mutations. For NRTIs, NNRTIs and PIs the prevalence of

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AUTHORS' CONTRIBUTIONS

Ziad El-Khatib (ZEK), Anna Mia Ekström (AME), Lerato Mohapi (LMi), Fatima Laher (FL), Alan Karstaedt (AK), Salome Charalambous (SC), Max Petzold (MP), David Katzenstein (DK) and Lynn Morris (LM) participated in the study design and ethics. Johanna Ledwaba (JL) did the genotyping and sequence analysis. ZEK, FL, AK, DK and LM participated in the study piloting and data collection. ZEK worked on the data analysis and the first manuscript. All authors participated in reviewing and commenting on the manuscript.

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mutations was 64%, 81% and 2% among first-line and 29%, 54% and 6% among second-line failures respectively. M184V/I, K103N and V106A/M were the most common mutations.

Significant risk factors associated with viremia on first-line included concurrent tuberculosis treatment (OR 6.4, 2.2-18.8, p<0.01) and a recent history of poor adherence (OR 2.7, 1.3-5.6, p=0.01). Among second-line failures, attending a public clinic (OR 4.6, 1.8-11.3, p<0.01) and not having a refrigerator at home (OR 6.7, 1.2-37.5, p=0.03) were risk factors for virological failure.

Conclusions: Risk factors for viral failure were line-regimen dependent. Second-line ART recipients had a higher rate of viremia, albeit with infrequent PI DR mutations. Measures to maintain effective virologic suppression should include increased adherence counseling, attention to concomitant tuberculosis treatment and heat-stable formulations of second-line ART regimens.

Keywords

Antiretroviral therapy; HIV; adherence; HIV drug resistance; South Africa; Viral failure

BACKGROUND

In South Africa, of the approximately 6 million HIV-1 infected individuals, more than 600,000 were enrolled into antiretroviral treatment (ART) programs by mid 2009 [1]. The majority of patients receive a first-line regimen that includes two nucleoside reverse-transcriptase inhibitors (NRTIs) and one non-NRTI (NNRTI). The NRTI drug, stavudine is routinely used although many patients show intolerability [2]. It is estimated that less than 10% of patients are on a second-line regimen that includes two NRTIs combined with one boosted protease inhibitor (PI) as recommend by the World Health Organization (WHO) [3,4]. While ART delays disease progression and premature death, sustained high adherence to ART is necessary to prolong viral suppression [5,6]. There are important consequences to viremia on first-line ART including the development of drug resistance mutations and the need to switch to a second-line regimen with considerable cost implications [7,8].

Although high levels of adherence to ART have been reported from small-scale HIV programs in sub-Saharan Africa [9,10], challenges arise as programs are taken to scale by governments in countries with a growing burden of HIV and tuberculosis (TB), limited health-care systems and drug supplies [11,12]. Many studies in southern Africa have examined virologic failure in different populations and shown that a number of factors influence viremia among first-line patients [13,14]. These include the HIV care setting, payment for ART, the distance traveled from home to clinic and adherence to appointments and medication among others. Some studies have also examined drug resistance (DR) among selected patients with virological failure and shown that the majority harbor mutations associated with lamivudine, NNRTIs and thymidine analogue mutations (TAMs) [13,15-18]. Here, we aimed to determine the relationship between prevalence of viremia, DR and reported adherence among ~1,000 long-term recipients of ART, including a proportion on 2nd line regimens, in Soweto, South Africa.

METHODS

Study setting

We conducted a cross-sectional study at two outpatient clinics at the Chris Hani Baragwanath Hospital, the largest hospital in Africa, located in Soweto outside Johannesburg serving a population of 4 million people [19,20]. Both clinics are affiliated to the Faculty of Health Sciences at the University of the Witwatersrand in Johannesburg and had access to ART through clinical research trials before the National ART scale-up in 2004. The first clinic is a non-governmental organization (NGO) research clinic [21] with

five medical doctors, three nurses, two nursing assistants and two counselors managing an estimated 50 HIV patients per day of the approximately 1,500 on ART (i.e. around 300 patients for each medical doctor). The second clinic is a public clinic with eight medical doctors, four nurses, one nursing assistant and seven counselors managing an estimated 200 HIV patient visits per day from approximately 3,500 on ART (i.e. around 440 patients for each medical doctor). The study was approved by the research ethics committees at the University of the Witwatersrand and the Regional Medical Ethics Board in Stockholm, Sweden. Written informed consent for conducting an interview and taking a blood sample was obtained from all patients.

Patient recruitment and interview

During March-September 2008, we recruited patients through posters in the clinic and pharmacy waiting areas in the three most widely spoken languages in Soweto: English, seSotho and isiZulu. Patients interested in the study were provided an information sheet, which included a 50 South African Rands ($5 US) as a transport reimbursement.

The following inclusion criteria were applied: 1) ≥18 years old; 2) being on ART ≥12 months; and 3) consenting to participate in the study. We initially enrolled 1,000 patients (500 at each site) but after discovering that two patients were interviewed twice at the public clinic the final number was 998 unique individuals.

The interview questionnaire was developed in English, translated into isiZulu and seSotho then back-translated to English. After piloting, the final questionnaire included 59 questions with a total of 210 items covering socio-economic background, disclosure, TB treatment, ART side-effects and adherence during the previous week-end [22] which served as a proxy for recent adherence. Two research assistants, trained in nursing and public health and fluent in all three languages, interviewed patients which took on average 15 minutes. The questionnaire data was entered into a database using EpiData [23,24]. A 10 ml blood sample was drawn by the clinic phlebotomist at the time of interview.

Laboratory assessments

CD4 counts were done on the day of blood draw using a BD FACSCount^{TM}. Plasma viral levels were assessed using the Roche Amplicor, version 1.5; Roche Diagnostics; lower limit of detection, 400 HIV RNA copies/ml.

For HIV genotyping, viral RNA was isolated from plasma samples with viral load (VL) >400 copies/ml using the MagNa Pure LC Total Nucleic Acid Isolation kit on the MagNa Pure Automated System (Roche Diagnostics) and sequenced using an in-house assay at the National Institute for Communicable Diseases (NICD) in Johannesburg [25]. Mutations were identified using the Stanford HIVdb genotypic resistance algorithm and then coded as major resistant mutations using the International AIDS Society (IAS) list from December 2009 [26]. HIV-1 subtype classifications were done using Rega v.2.0 [27].

Data analysis

We grouped patients per type of line regimen, i.e. first-line and second-line, then a number of variables were examined as potential predictors of viremia. For each variable we first calculated the adjusted odds ratio (adj. OR 95% CI) and p-value controlling for gender, education, type of clinic, age and self-reported adherence during the last week-end, which is denoted as the basic adjusted model. The presented adj. OR for the five variables in the previous sentence are derived from a regression model including only these covariates.

All variables with p-values ≤0.15 in the basic adjusted model, were added into a backward selection multiple logistic regression analysis (inclusion criteria was p≤0.05) This model is denoted the final model. The adherence variable was included in the model regardless of p-value. Stata/SE College Station, Texas (version 10.1) was used for data analysis [30].

RESULTS

Patient characteristics

A total of 998 HIV-1 infected subjects receiving ART at either an NGO or public clinic at the same hospital were interviewed for this study (Table 1A). The majority of the patients were women (75%), who, with a median age of 41 years, were significantly older than the men (median age 37 years) (p<0.001). Overall, 78% had attained some secondary education, 64% lived in a house, 24% lived in an informal dwelling (shack), and 13% did not own a refrigerator. More than half of the study population was in a partner relationship, 14% were married, ~14% cohabitated and 24% reported a sexual relationship but lived alone. Only 3% of all patients reported more than one (>1) sexual partner during the last 3 months and the majority reported using condoms consistently. Seventy percent of patients were unemployed and 7% were working in casual or daily labour. Forty percent of the subjects relied on receipt of a disability grant from social services of 940 South African Rands (around $122US) per month. Only 38% did not rely on others for monetary support. The vast majority (91%) of patients used public transport to attend outpatient ART clinics.

There were significant differences in the patient populations between the two clinical sites. At the public clinic there was a higher percentage of men, patients were older, single, lived in informal dwellings, were poor and more likely to be unemployed compared to patients attending the NGO clinic (p<0.01 for all of the above variables).

Treatment and viremia

More than half (64%) of the study population had been on ART for longer than 36 months (p<0.01) (Table 1B). The majority (89%) were on an NNRTI–based (first-line) and 12% were on a PI-based (second-line). A larger proportion of patients were on second-line therapy at the NGO clinic consistent with this site having a more ART-experienced population. Five percent of patients reported having missed taking their pills during the previous weekend and were classified as incompletely adherent. This was more apparent for the patients attending the NGO clinic (p=0.03).

Although more than 50% of all subjects reported previous treatment for TB, only 2% (n=18) were receiving TB therapy at the time of study. Among the 14 first-line recipients who were on TB therapy, 13 were on stavudine, lamivudine and efavirenz and one was on zidovudine, lamivudine and efavirenz. We found no significant difference in either median time on ART or median CD4 cell count for TB versus non-TB patients (data not shown).

At enrolment into the study, the median CD4 count for the group was 383 cells/μl (range 1-1,770). Viremic patients had a significantly lower CD4 count (214 cells/μl; range 1-764) compared to those who were suppressed (414 cells/μl; range 40-1,770) (p<0.001). Those at the public clinic had lower CD4 counts.

Of the 998 patients, 139 (14%) had a VL >400 copies/ml and were therefore defined as viremic on ART, with a median of 10,500 copies/ml (range 407 - 1,000,000). There was a higher prevalence of viremic patients at the public clinic compared to the NGO clinic (17% vs. 11%, p=0.01). Of the viremic patients, 102 were on first-line therapy and 37 were on a second-line regimen with a significant difference in median viral levels (6,540 vs. 24,400 copies/ml respectively, p=0.01).

Prevalence of HIV- drug resistance

Among the 139 patients with viremia, 129 (93%) plasma samples with a median VL of 13,500 copies/ml were successfully genotyped versus 10 samples with a median of 2,025 copies/ml that could not be amplified [28] (p=0.04). Of the successfully sequenced samples, 128 were HIV-1 subtype C and one was subtype B.

Seventy-eight percent of viremic patients had at least one DR mutation and 52% (67/129) harboured both NNRTI and NRTI resistance mutations (Table 2). Of the 94 viremic patients on the first-line regimen, 64% (n=60), 81% (n=76), and 2% (n=2) had evidence of NRTI, NNRTI, and PI resistance respectively; M184V/I and K103N were the most prevalent mutations (62% (n=58) and 48% (n=45) respectively), and 16% (n=15) had TAMs. Among the 35 viremic patients failing a second-line regimen, 29% (n=10), 54% (n=19) and 6% (n=2) patients had mutations associated with NRTI resistance (mainly M184V/I, n=9), NNRTI resistance (mainly K103N, n=15), and major PI mutations respectively. The two patients with PI mutations harboured either Q58E, L90M or N88S. All PI recipients were on lopinavir/ritonavir, except for one patient receiving ritonavir and atazanavir.

There were no significant differences in the frequency of mutations in samples with viral level below or above 5,000 copies/ml (78% vs. 65% respectively, p=0.10) which is the recommended cut-off for switching adult patients failing first-line regimens in the South African clinical guidelines at the time of the study [4].

Risk factors for viremia

In order to determine factors associated with viremia we performed a multiple logistic regression analysis using a full and a reduced model (see Methods for description). Among 883 patients on a first-line regimen, viremia was significantly associated with self-reported poor adherence (OR 2.7, 95% CI 1.3-5.6, p=0.01) during the previous weekend and being on TB treatment in both models (OR 6.4, 95% CI 2.2-18.8, p<0.01) (Table 3). There was no significant association between viremia and gender, type of clinic and duration of treatment for those on first-line ART. In addition we found no significant association between viremia and age, education level, being unemployed or income level (data not shown).

For the 115 patients on a second-line regimen there was a higher risk of virological failure associated with attending the public clinic (OR 4.6, 95% CI 1.8-11.3, p<0.01) and not having a refrigerator at home (OR 6.7, 95% CI 1.2-37.5, p=0.03). In the basic adjusted model, receipt of TB treatment was significantly associated with viremia (p<0.01). Since all four TB patients were viremic it was not possible to fit the final model. There was no risk of viremia associated with reported incomplete adherence during the previous weekend (OR 2.8, 95% CI 0.4-19.6, p=0.29) unlike what was seen among first-line failures.

Further analysis was done among patients failing first-line therapy with either DR mutant or wild-type viremia. Ninety-six percent (96%) of those with DR mutations reported good adherence. In contrast, only 63% of patients exhibiting wild-type virus reported good adherence (p<0.01, data not shown).

DISCUSSION

In this cross-sectional study among nearly 1,000 South African HIV-1 infected patients where the majority had been on ART for more than three years, we found a 14% prevalence of viremia, 78% of whom had HIV DR strains. As anticipated, self-reported lapses in adherence to ART were strongly associated with viremia. Furthermore, ongoing TB treatment was a risk factor for failing first-line ART. Among second-line ART recipients, virological failure was associated with attending a larger, less resourced public clinic and

not owning a refrigerator. Nevertheless, despite poor socio-economic conditions, the majority of patients in this study were fully suppressed and highly adherent after many years on ART.

The strongest predictor for viremia was concomitant TB treatment, which may relate to multiple factors such as reduced ART adherence during severe illness, increased pill burden, exacerbation of side effects, and drug interactions with rifampicin which may reduce NNRTI and PI levels in plasma concentrations [29]. While studies have not focused specifically on adherence to ART among TB patients, we suspect that adherence to concomitant ART and TB treatment is made difficult for patients when care is not integrated which increases waiting times and transport costs. In a recent review by Lawn and co-workers, TB incidence rates on ART were shown to decrease over time, but baseline CD4 cell count, gender and socioeconomic conditions still influenced TB acquisition on ART [30]. Given that UNAIDS reports that more than half of TB patients are HIV infected and that in this study most patients had previously received TB treatment, better integration of HIV and TB care should be encouraged [31].

Not all patients in this study who reported recent poor adherence were viremic at the time of the interview. This may confirm the findings of Rosenblum and co-workers who showed that the longer patients are virologically suppressed on ART, the less likely they are to become viremic after missing taking any of their pills [32]. The increased frequency of virologic failure among patients at the public clinic may reflect the higher workload, higher patient-to-provider ratio and more limited-resources in the public sector. Fielding and co-workers made a similar finding when comparing 39 HIV clinics in South Africa that used the same clinical guidelines. They speculate that this is related to long waiting times at the clinic and/or pharmacy and lack of resources to follow-up patients for their clinic/drug refill appointments [14]. In addition, the patients attending the public clinic were more financially and socially vulnerable compared to their peers at the NGO clinic; however they reported higher adherence levels compared to the NGO clinic. We found that patients who did not own a refrigerator were more likely to fail their second-line regimen. Lopinavir/ritonavir currently used in South Africa, prescribed as three pills to be taken twice per day, is a soft gel capsule requiring refrigeration, highlighting the need for a heat-stable formulation particularly in areas with poor socio-economic conditions.

Among viremic patients, 78% had resistance mutations and the mutational patterns were similar to recently reported studies from South Africa [15,16,33-35] and other limited-resource countries that use the same first-line regimens [13,33-38]. Thus, M184V/I, K103N and V106A/M were the most common mutations due to lamivudine and NNRTI use. However, in contrast to three other studies from South Africa there was a relatively lower prevalence of TAMs [15,16,18]. Interestingly, among patients failing second-line ART, most were found to harbour DR mutations associated with failure of line-one regimens (particularly the NNRTI mutation, K103N), and there was an extraordinary paucity of PI related mutations. This suggests the inability of lopinavir/ritonavir to select PI resistance mutations at high levels as noted by others [39,40] and re-emergence of archived mutations from first-line NNRTI regimens.

There are several limitations to this cross-sectional study. A recent review showed that as many as 50% of patients die or are lost to follow-up during the first 24 months on ART in sub-Saharan Africa [41]. Thus, the patients studied here may represent those who were the most adherent and who remained in treatment which reduces the sensitivity of identifying risk factors associated with failure. A further caveat is that the use of self-reported missed doses over the previous weekend as a proxy for adherence. While adherence is known to change over time [42], this measure has been successfully used by others [10,19,43-45].

Given the long-term treatment nature of this cohort and the possibility of recall bias, we chose to use this indicator which was predictive, at least among first-line ART recipients. Patients were recruited through invitation, and we only captured an estimated 10-20% of eligible patients while attending either the clinic or the pharmacy, and thus was not a random sampling. However, the demographic characteristics, including gender, age and marital status, of our study participants are consistent with national statistics and were similar to a larger number studied by Rosen at multiple-sites in South Africa [46]. The rate of detection of viremia was consistent with a recent report from South Africa, of viremia on ART after 12 months [14]. We were unable to adjust for baseline viral load, CD4 and DR as this data was not available on all subjects. However, the prevalence of transmitted ART resistance among South African patients initiated on ART 2-5 years ago is likely to be low (<5%) [28,47].

We found that the majority of viremic patients who were failing their first-line regimen already had regimen specific DR, irrespective of their viral load level. This confirms Aleman and co-workers findings that DR mutations may occur among viremic patients at low and stable viral load level [48]. These findings underscore the importance of viral load monitoring to identify treatment failure. National guidelines mandate that those with viremia on a first-line regimen be switched to a second-line regimen. Our data showed that approximately a quarter of patients failed without evidence of major DR mutations. These individuals may re-suppress with adherence to first-line drugs [17] although the presence of minority quasispecies may compromise treatment outcomes [49] and thus the most appropriate intervention may be to switch to a second-line regimen even in cases of wild-type viremia.

In summary, risk factors for virological failure were line-regimen dependent. Increased attention to adherence particularly among those receiving concomitant TB treatment may reduce virologic failure among first-line ART recipients. With the availability of regular subsidised VL assessments, the public health care system in South Africa can identify viremia and initiate second-line treatment. However, further clinical research is needed to identify the causes of second-line failure and to improve the response to second-line regimens with alternatives to lopinavir/ritonavir-based treatment. Assessment of drug resistance, in addition to VL monitoring and adherence counselling before a change in therapy, warrants further investigation.

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Table 1

Patients' characteristics

	Overall		By type of clinic		
A. Demographic information	**N**	**%**	**NGO N (%)**	**Public N (%)**	**p value**
Gender					
Women	744	74.6%	388 (77.6%)	356 (71.5%)	
Men	254	25.4%	112 (22.4%)	142 (28.5%)	0.03
Age					
≤34	312	31.3	176 (35.2%)	136 (27.3%)	
35-44	462	46.3	225 (45%)	237 (47.6%)	0.03
≥45	224	22.4	99 (19.8%)	125 (25.1%)	<0.01
Highest education level					
Never been to school	14	1.4%	8 (1.6%)	6 (1.2%)	
Primary school	145	14.5%	44 (8.8%)	101 (20.3%)	0.04
Secondary school	779	78.1%	413 (82.6%)	366 (73.5%)	0.76
Tertiary	60	6%	35 (7%)	25 (5%)	0.93
Type of housing					
House	639	64.1%	340 (68.1%)	299 (60%)	
Informal dwelling (shacks)	241	24.2%	92 (18.4%)	149 (29.9%)	<0.01
Other (either flat, shared room or other)	117	11.7%	67 (13.5%)	50 (10.1%)	0.42
Have refrigerator in the household					
Yes	868	87%	415 (83.3%)	453 (90.6%)	
No	130	13%	83 (16.7%)	47 (9.4%)	0.01
In a relationship					
No (single, divorced, separated, widow)	482	48.4%	205 (41.2%)	277 (55.7%)	
Yes (married, sex partner, cohabitation)	513	51.6%	293 (58.8%)	220 (44.3%)	<0.01
Number of sexual partners last 3 months					
0	325	32.7%	146 (29.3%)	179 (36.2%)	
1	644	64.8%	339 (67.9%)	305 (61.6%)	0.02
2-4 partners	25	2.5%	14 (2.8%)	11 (2.2%)	0.28
If >1 partner, did you use condoms					

	Overall		By type of clinic		
A. Demographic information	**N**	**%**	**NGO N (%)**	**Public N (%)**	**p value**
All the time	21	84%	12 (85.8%)	9 (81.8%)	
Sometimes	3	12%	1 (7.1%)	2 (18.2%)	0.44
No, not at all	1	4%	1 (7.1%)	0	0.39
Employment status					
Not employed	648	70.3%	309 (64.5%)	339 (76.5%)	
Employed	274	29.7%	104 (35.3%)	170 (23.5%)	<0.01
Income - < median level = US$ 122	609	61%	264 (52.8%)	345 (69.3%)	<0.01
On child support grant					
No	729	73.7%	346 (70%)	383 (77.4%)	
Yes	260	26.3%	148 (30%)	112 (22.6)	<0.01
Transport to clinic					
Public transport	904	90.8%	447 (89.4%)	457 (92.1%)	
Walking	52	5.2%	26 (5.2%)	26 (5.2%)	0.94
Own car	35	3.5%	23 (4.6%)	12 (2.4%)	0.06
Other	5	0.5%	4 (0.8%)	1 (0.2%)	0.17
B. Clinical characteristics	**N**	**%**	**NGO**	**Public**	**p value**
Time on ART (by months)					
12-23 months	154	15.4%	22 (4.4%)	132 (26.5%)	
24-36 months	207	20.7%	41 (8.2%)	166 (33.3%)	0.17
>36 months	637	63.9%	437 (87.4%)	200 (40.2%)	<0.01
Line regimen					
NNRTI based (i.e. first-line)	883	88.5%	431 (86.2%)	452 (90.8%)	
PI based (i.e. second-line)	115	11.5%	69 (13.8%)	46 (9.2%)	0.02
Missed any pills during last week-end					
No	941	95%	465 (93.6%)	476 (96.5%)	
Yes	49	5%	32 (6.4%)	17 (3.5%)	0.03
Currently on TB treatment - yes	18	1.8%	10 (2%)	8 (1.6%)	0.64
CD4 cell count					

	Overall		By type of clinic		
A. Demographic information	**N**	**%**	**NGO N (%)**	**Public N (%)**	**p value**
<=200 cells/μl	137	13.7%	47 (9.4%)	90 (18.1%)	
>200 cells/μl	861	86.3%	408 (90.6%)	453 (81.9%)	<0.01
VL >400 HIV RNA copies/ml	139	13.9%	55 (11%)	84 (16.9%)	0.01
NNRTI based	102	73.4%	43 (78.2%)	59 (70.2%)	
PI based	37	26.6%	12 (21.8%)	25 (29.8%)	0.30

Table 2

Number and type of HIV-1 drug resistance mutations

Mutation	Number (%) of patients	
	First-line regimen	Second-line regimen
NRTI resistance	**N=94**	**N=35**
Any NRTI mutations	60 (63.8%)	10 (28.6%)
M184V/I	58 (61.7%)	9 (25.7%)
TAMs	15 (16%)	2 (5.7%)
D67N	11 (11.7%)	1 (2.9%)
T215Y/F	5 (5.3%)	1 (2.9%)
K70R	4 (4.3%)	1 (2.9%)
K219Q/E	4 (4.3%)	1 (2.9%)
M41L	3 (3.2%)	0
A62V	3 (3.2%)	0
V75I	3 (3.2%)	0
K65R	1 (1.1%)	0
L74V	1 (1.1%)	0
L210W	1 (1.1%)	0
NNRTI resistance		
Any NNRTI mutation	76 (80.8%)	19 (54.3%)
K103N	45 (47.9%)	15 (42.9%)
V106A/M	25 (26.6%)	2 (5.7%)
G190S/A	13 (13.8%)	1 (2.9%)
Y188C/L/H	13 (13.8%)	1 (2.9%)
K101E/H/P	12 (12.8%)	1 (2.9%)
P225H	10 (10.6%)	5 (14.3%)
Y181C/I/V	3 (3.2%)	0
L100I	1 (1.1%)	0
PI resistance		
Any PI mutation	2 (2.1%)	2 (5.7%)
Q58E	1 (1.1%)	1 (2.9%)
M46L	1 (1.1%)	0
L90M	0	1 (2.9%)
N88S	0	1 (2.9%)
Any resistance mutation	101/129 (78.3%)	
NNRTI and NRTI resistance	67/129 (52.0%)	
NRTI and PI resistance	2/129 (1.6%)	
NNRTI, NRTI and PI resistance	0	

AIDS. Author manuscript; available in PMC 2011 July 17.

Table 3

Risk factors for viremia

Patients' Characteristics			Basic adjusted model		Final model	
	VL>400 RNA copies/ml	VL<400 RNA copies/ml	Adj. OR (95% CI)*	P value	OR (95% CI)	P Value
NNRTI based regimen						
Gender						
Men	30 (12.7%)	207 (87.3%)	1			
Women	72 (11.2%)	573 (88.8%)	0.9 (0.6-1.5)	0.75		
Missed any pills during last week-end						
No	92 (90.2%)	740 (95.8)	1		1	
Yes	10 (9.8%)	32 (4.2%)	2.5 (1.2-5.4)	0.02	2.7 (1.3-5.6)	0.01
On a child support grant						
No	68 (10.4%)	584 (89.6%)	1			
Yes	33 (14.9%)	189 (85.1%)	1.6 (0.9-2.6)	0.08		
On a disability grant						
No	58 (10.9%)	473 (89.1%)	1			
Yes	43 (12.5%)	300 (87.5%)	1.2 (0.8-1.9)	0.40		
Type of clinic						
NGO	43 (10%)	388 (90%)	1			
Public	59 (13.1%)	392 (86.9%)	1.4 (0.9-2.2)	0.12		
Currently on TB treatment						
No	96 (11.2%)	772 (88.9%)	1		1	
Yes	6 (42.9%)	8 (57.1%)	7.0 (2.3-20.9)	<0.01	6.4 (2.2-18.8)	<0.01
Have refrigerator in the household						
Yes	85 (11.2%)	675 (88.8%)				
No	17 (14%)	104 (86%)	1.1 (0.6-2.1)	0.71		
Time on ART						

Patients' Characteristics			Basic adjusted model		Final model	
	VL>400 RNA copies/ml	VL<400 RNA copies/ml	Adj. OR (95% CI)*	P value	OR (95% CI)	P Value
NNRTI based regimen						
12-23 months	22 (14.3%)	132 (85.7%)	1			
24-36 months	24 (13.3%)	157 (86.7%)	1.0 (0.5-1.8)	0.93		
≥ 37 months	56 (10.2%)	491 (89.8%)	0.8 (0.4-1.4)	0.46		
PI based regimen						
Gender						
Men	10 (58.8%)	7 (41.2%)	1			
Women	27 (27.5%)	71 (72.5%)	0.5 (0.2-1.6)	0.24		
Missed any pills during last week-end						
No	34 (92%)	74 (94.9%)	1			
Yes	3 (8.1%)	4 (5.1%)	2.8 (0.4-19.6)	0.29		
On a child support grant						
No	30 (39.5%)	46 (60.5%)	1			
Yes	7 (18.4%)	31 (81.6%)	0.5 (0.2-1.5)	0.23		
On a disability grant						
No	30 (39.5%)	46 (60.5%)	1			
Yes	7 (18.4%)	31 (81.6%)	0.9 (0.4-2.3)	0.89		
Type of clinic						
NGO	12 (17.4%)	57 (82.6%)	1		1	
Public	25 (54.3%)	21 (45.7%)	5.8 (2.1-16.1)	<0.01	4.6 (1.8-11.3)	<0.01
Currently on TB treatment						
No	33 (29.7%)	78 (70.3%)	1			
Yes	4 (100%)	0	NA	0.01		
Have refrigerator at the household						
Yes	30 (28.3%)	76 (71.7%)			1	

Patients' Characteristics			Basic adjusted model		Final model	
	VL>400 RNA copies/ml	VL<400 RNA copies/ml	Adj. OR (95% CI)*	P value	OR (95% CI)	P Value
NNRTI based regimen						
No	7 (77.8%)	2 (22.2%)	4.2 (0.7-26.8)	0.10	6.7 (1.2-37.5)	0.03
Time on ART						
12-23 months	0	0				
24-36 months	11 (42.3%)	15 (57.7%)	1			
≥ 37 months	26 (29.2%)	63 (70.8%)	0.7 (0.3-2.1)	0.56		

*Adjusted for gender, education, clinic type, age and adherence during the week-end prior to the study interview