with someone who is infected?; (6) Can a person get HIV through injections with a needle that was already used by someone else?; (7) Can people who inject drugs protect themselves from HIV by switching to non-injecting drugs?; (8) Can a pregnant woman infected with HIV transmit the virus to her unborn child?; and (9) Can a woman with HIV transmit the virus to her newborn child through breastfeeding? All of these questions were given in a Likert scale with options of "yes", "no" and "do not know".

HIV testing

After completing the interview, blood samples were collected from each study participant by finger prick blood sampler complying with the National HIV Testing Protocol. Considering the availability of limited human and financial resources, the Ministry of Health and Population of Nepal has recommended the use of two or more rapid tests based on different test principles (antigens) as a minimum standard HIV test algorithm to be followed at all levels of the health care delivery system [28]. Two rapid test kits Determine HIV 1/2 and Uni-Gold HIV 1/2 were used for the purpose. The initial screening test was performed using Determine HIV 1/2 and then retested using the Uni-Gold HIV 1/2 when the first test result was positive for confirmation. A third test SD Bioline HIV 1/2 was performed for final confirmation when there was discrepancy in the first two tests. If the third test showed a reactive result, the tested sample was reported as "HIV positive" and if the third test showed a non-reactive result, it was reported as "HIV negative". Sensitivity and specificity of combined testing algorism of Determine and SD Bioline are reported to be both 100% [29,30]. The HIV test results were kept confidential. Pre-test counselling was provided as a part of informed consent and the participants were informed of the testing result only at post-test counselling.

Ethical issues

This research protocol was approved by the Nepal Health Research Council and the Committee for Research on Human Subjects at Kyoto University in Japan. Separate written informed consents were obtained for the interview and HIV testing, and no personal identifier was recorded on the questionnaires. All the participants were advised to undertake free HIV testing for final clinical diagnosis.

Statistical analysis

Statistical analyses were carried out using SPSS software for Windows (version 19, IBM Inc., Chicago). Bivariate analyses were conducted to estimate the association of demographic or behavioural variables with HIV infection, calculating crude odds ratio (OR) with 95% confidence interval (CI). Multiple multivariate models were run: (a) to compare the predictive powers of behavioural variables of different time frames; and (b) to show independent correlates to HIV infection. The significant variables from bivariate analyses, epidemiologically important variables and synthetic variables created by combining related variables were included in the models. Independent variables were assessed for multicollinearity, variance inflation factor and tolerance statistics were within acceptable limits for all variables [31]. From multivariate models adjusted odds ratio (AOR) and 95% CI were calculated. A p-value less than 0.05 (2-sided) was considered to be statistically significant. Answers to the HIV knowledge questions were transformed into scores by giving 1 for correct answer and 0 for otherwise.

Results

A total of 269 participants were included in the analysis, of whom 28.6% were HIV positive. The major socio-demographic characteristics of the participants are shown in Table 1.

More than half (52.0%) of the study participants were recruited in the streets. No association was detected between sites of recruitment and HIV status of the participants ($p = 0.98$). More than half of the participants (57.6%) were under 25 years old; the median age being 23 years. HIV infection was found to be associated with older age groups; the prevalence being 50.0% in the 30 years and above. The majority (76.2%) of the participants were married and/or cohabitating with their sexual partners, which is highly associated with HIV infection ($p = 0.002$ or $p < 0.001$). More than 80% of the participants had ever been to school, and the HIV prevalence (34.1%) is much higher in this group than those without school education (4.1%) ($p = 0.001$). Although 53.3% of the participants were unemployed, the job situation of the participants was unrelated to the HIV status ($p = 0.307$).

Table 2 shows the prevalence of risky behaviours in this population and the results of bivariate analyses between HIV status and HIV/STI knowledge score or behavioural variables. Risky behaviours are highly prevalent in this population. Injection practice in lifetime was reported from 78.4% (211/269); of them 24.2% (51/211) shared needles and/or syringes most times or always, and 86.7% (183/211) had shared a cooker or other utensils sometimes or more with other people in the past one month. Sex with regular, non-regular non-commercial partners (herein after "casual partners") and commercial partners were reported by 74.1% (166/224), 45.5% (102/224) and 58.5% (131/224) of sexually active participants respectively. Among them 79.5% (132/166), 75.5% (77/102) and 87.8% (115/131) reported that they are not always using condoms, respectively.

All these variables are significantly associated with increased risk of HIV infection except for HIV knowledge.

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Table 1 Socio-demographic characteristics of female drug users with or without HIV infection recruited in the Kathmandu Valley, Nepal

	Positive HIV test (n = 77) n (%)	Total (n = 269)	Crude OR (95% CI)	p value
Place of recruitment				
Street/Park	40 (28.6)	140	1.00	
Drop in centre	37 (28.7)	129	1.01 (0.59-1.71)	0.984
Age (years)				
16 - 19	7 (25.9)	27	1.00	
20 - 24	25 (19.5)	128	0.69 (0.26-1.82)	0.457
25 - 29	28 (35.0)	80	1.54 (0.58-4.08)	0.387
30 - 38	17 (50.0)	34	2.86 (0.96-8.52)	0.060
Mean (SD) (Median)	26.3 (6.0) (25.0)	24.4 (4.8) (23.0)	1.12 (1.06-1.18)	<0.001
Marriage and live-in partnerships				
Not married, not living with sexual partner	6 (9.4)	64	1.00	
Not married, living with sexual partner	25 (32.5)	77	4.65 (1.77-12.22)	0.002
Currently married, not living with spouse or any other sexual partner	12 (36.4)	33	5.52 (1.84-16.59)	0.002
Currently married, living with spouse or other sexual partner	34 (35.8)	95	5.39 (2.11-13.79)	<0.001
Level of education				
Never went to school	2 (4.1)	49	1.00	
Primary (1–5 years)	15 (48.4)	31	22.03 (4.54-107.04)	<0.001
Secondary (6–10 years)	26 (27.4)	95	8.86 (2.01-39.10)	0.004
Higher (11 years and higher)	34 (36.2)	94	13.32 (3.04-58.28)	0.001
Job situation				
Have a job	32 (25.6)	125	1.00	
Jobless	45 (31.3)	144	1.32 (0.77-2.25)	0.307

SD, standard deviation.
OR, odds ratio.
CI, confidence interval.

The prevalence of HIV is high among those who had ever injected (OR = 3.04, p = 0.006) as well as among those who ever used needle or syringes previously used by someone else (OR = 3.08, p < 0.001). Frequency of injection in the past one month is associated with positive HIV status in a dose-dependent manner; the participants injecting once or more a day have the highest (39.2%) HIV prevalence (OR = 4.03, p = 0.001). Frequency of sharing injection instruments or other accessory utensils such as a cooker in the past one month is also associated with positive HIV status but not in a dose-dependent manner. Sexual experiences, both over a life time and in the last 12 months, are strongly associated with HIV status with equivalent magnitudes (OR = 10.82 and 9.13, p ≤ 0.001). Similarly, sexual experience with any type of partner in the past 12 months is strongly associated with the HIV status (OR = 3.50-5.91, p < 0.001) with the highest association being with casual partners. The majority of the participants used condoms inconsistently with any type of sexual partner. The frequency of condom use with a regular partner or casual partner is associated with HIV status in a dose-dependent manner. The prevalence is highest among the participants who never or only sometimes used condoms with their regular partners (40.4%, OR = 3.97, p < 0.001) or casual partner (55.2%, OR = 6.99, p < 0.001). The frequency of condom use with commercial partners is also significantly associated with the HIV status but not in a dose-dependent manner.

Table 3 summarizes the results of multivariate analyses of factors associated with HIV infection. Multiple logistic regression analyses were carried out using behavioural variables with different time frames as well as synthetic variables with different risk specificities. This analytic strategy was adopted because although some questions were asked in an "ever" time frame for injection and sexual behaviours, the rest of the questions were asked in different time frames; "in the past one month" for drug use and "in the past 12 months" for sexual behaviours. It seemed therefore necessary to assess the effect of the time frame on the predictive power

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Table 2 Bivariate association of behavioural factors with HIV infection among female drug users recruited in the Kathmandu Valley, Nepal

	Positive HIV test (n = 77) n (%)	Total (n = 269)	Crude OR (95% CI)	p value
HIV Knowledge scores				
6 - 9	66 (27.8)	237	1.00	
0 - 5	11 (34.4)	32	1.36 (0.62-2.97)	0.445
Drug use behaviour				
Ever injected illegal/non-medical drugs				
No	8 (13.8)	58	1.00	
Yes	69 (32.7)	211	3.04 (1.37-6.76)	0.006
Ever used a needle or syringe previously used by someone else				
No/Non-IDU	23 (17.4)	132	1.00	
Yes	54 (39.4)	137	3.08 (1.75-5.43)	<0.001
Frequency of injecting with a needle or syringe previously used by someone else in the past one month				
Non-IDU/Never	24 (17.5)	137	1.00	
Occasionally/About half the time	36 (44.4)	81	3.77 (2.02-7.01)	<0.001
Always/Most times	17 (33.3)	51	2.35 (1.13-4.89)	0.022
Frequency of sharing cooker/vial/container, cotton/filter, or rinse water when injecting in the past one month				
Never/Non-IDU	19 (22.1)	86	1.00	
Sometimes	17 (21.8)	78	0.98 (0.47-2.06)	0.963
Always/Often	41 (39.0)	105	2.26 (1.19-4.30)	0.013
Frequency of injecting drugs in the past one month				
Non-IDU	8 (13.8)	58	1.00	
6 times a week or LESS	9 (15.5)	58	1.15 (0.41-3.22)	0.793
1 time a day or MORE	60 (39.2)	153	4.03 (1.79-9.10)	0.001
Sexual behaviour				
Ever had sexual intercourse				
No	2 (4.4)	45	1.00	
Yes	75 (33.5)	224	10.82 (2.55-45.89)	0.001
Sexual intercourse in the last 12 months with any type of partner				
No/Never had sex	4 (5.9)	68	1.00	
Yes	73 (36.3)	201	9.13 (3.19-26.08)	<0.001
Sexual intercourse with regular partner in the last 12 months				
No/Never had sex	15 (14.6)	103	1.00	
Yes	62 (37.3)	166	3.50 (1.86-6.58)	<0.001
Sexual intercourse with commercial partner in the last 12 months				
No/Never had sex	19 (13.8)	138	1.00	
Yes	58 (44.3)	131	4.98 (2.75-9.02)	<0.001
Sexual intercourse with non-regular non-commercial partner in the last 12 months				
No/Never had sex	25 (15.0)	167	1.00	
Yes	52 (51.0)	102	5.91 (3.32-10.51)	<0.001

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Table 2 Bivariate association of behavioural factors with HIV infection among female drug users recruited in the Kathmandu Valley, Nepal *(Continued)*

Frequency of condom use in the last 12 months with all regular partners				
Never had sex/No sex with regular partner in the last 12 months	15 (14.6)	103	1.00	
Always/Often	20 (32.3)	62	2.79 (1.30-6.00)	0.008
Sometimes/Never	42 (40.4)	104	3.97 (2.03-7.79)	<0.001
Frequency of condom use in the last 12 months with all commercial partners				
Never had sex/No sex with commercial partner in the last 12 months	19 (13.8)	138	1.00	
Always/Often	36 (54.5)	66	7.52 (3.79-14.91)	<0.001
Sometimes/Never	22 (33.8)	65	3.20 (1.58-6.49)	0.001
Frequency of condom use in the last 12 months with all non-regular non-commercial partners				
Never had sex/No sex with casual partner in the last 12 months	25 (15.0)	167	1.00	
Always/Often	20 (45.5)	44	4.73 (2.28-9.82)	<0.001
Sometimes/Never	32 (55.2)	58	6.99 (3.58-13.66)	<0.001

Non-IDU, non-injecting drug user.
OR, odds ratio.
CI, confidence interval.

of the variables. It was also expected that the predictive power of the variables would be enhanced by creating synthetic variables to represent more directly the risk of behaviours.

Models 1 to 6 include all drug users but model 7 includes only injecting drug users. "Ever injected illegal/non-medical drugs" and "Ever had sexual intercourse" were entered in model 1, while the latter was replaced with "Had sexual intercourse in the last 12 months" in model 2 showing that association of sexual behaviour is more prominent "in the last 12 months" than "ever". In models 3 and 4, on the other hand, a variable "Ever injected illegal/non-medical drugs" was replaced with a variable "Ever used needles or syringes previously used by someone else" (model 3) or a synthetic variable "Used needles or syringes previously used by someone else in the past one month" (model 4), while keeping the variable "Ever had sexual intercourse" the same as in model 1. From the comparison of models 1 to 4, it was shown that all injection variables had equivalent predictive power (AOR = 2.5) irrespective of time frame or the presence/absence of sharing practice, and that sexual variables had predictive powers that were equivalent to or more potent than the injection variables among the participants.

Model 5 is an extension of model 2 where the risks of sexual intercourses with different types of partners in the past 12 months with HIV infection were compared. While significant association was detected for sexual intercourses with commercial and casual partners, it was not significant with regular partners. Model 6 is the extension of model 4 using a synthetic variable where "Used needles or syringes previously used by someone

else in the past one month" was combined with the frequency of injection in the past month. It was shown that frequent unsafe injection practice (sharing needles and syringes once a day or more) and frequent unsafe sex (intercourses with 'sometimes or never' condom use) with casual partners were significantly associated with HIV infection, while with commercial sexual partners intercourses with 'always or often' rather than infrequent condom use showed significant association. Such an association pattern was maintained when analysis was confined to female injecting drug users (model 7). Throughout these models, age and "Ever attended school" but not "Marital status" were significantly associated with HIV infection. "Ever attended school" was the most potent predictor of HIV infection, while its association nearly halved when sexual behaviour variables were switched from the general ones to those specific to sexual partners. Behavioural and injecting practice variables were introduced in the order of all possible combinations into models 5 through 7, yielding similar results.

Discussion

Overall, HIV prevalence in this population was revealed to be 28.6%; 33% in those who practised injecting drug use and 14% even among those who reportedly never experienced injecting drug use. In Nepal, the Integrated Biological and Behavioral Surveillance (IBBS) surveys are conducted at regular intervals among male IDUs. The latest round of IBBS showed a significant decline in HIV prevalence among male IDUs in Kathmandu Valley, from 51.7% in 2005 to 6.3% in 2009 [10], which is much lower than the HIV prevalence we found among female IDUs. This study strongly suggests that female drug users are

Table 3 Multivariate association of behavioural factors with HIV infection among female drug users in the Kathmandu Valley, Nepal

	All drug users						Only IDUs
	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6	Model 7
	Adjusted odds ratio						
	(95% confidence interval)						
Age	1.10*	1.10*	1.11*	1.11*	1.07*	1.07	1.08*
	(1.04-1.17)	(1.03-1.17)	(1.04-1.18)	(1.04-1.19)	(1.01-1.15)	(1.00-1.15)	(1.00-1.17)
Ever attended school (ref. No)	10.85*	9.03*	10.83*	10.52*	6.14*	6.21*	4.85
	(2.46-47.79)	(2.05-39.73)	(2.44-48.13)	(2.38-46.56)	(1.34-28.06)	(1.31-29.49)	(0.96-24.55)
Currently married, or currently not married but living with sex partner (ref. Not married, not living with sexual partner)	2.33	2.15	1.84	1.85	2.01	1.62	1.69
	(0.72-7.53)	(0.78-5.94)	(0.57-5.96)	(0.57-6.01)	(0.72-5.66)	(0.57-4.62)	(0.52-5.47)
Ever injected illegal/non-medical drugs (ref. No)	2.48*	2.41*			2.65*		
	(1.05-5.84)	(1.02-5.73)			(1.08-6.49)		
Ever used a needle or syringe previously used by someone else (ref. No/Non-IDU)			2.50*				
			(1.35-4.63)				
Used needles or syringes previously used by someone else in the past one month (ref. Never/non-IDU)				2.60*			
				(1.40-4.81)			
Used needles or syringes previously used by someone else, injecting 6 times a week or less in the past month (ref. Non-IDU/Never)						0.93	0.78
						(0.24-3.64)	(0.19-3.26)
Used needles or syringes previously used by someone else, injecting 1 time a day or more in the past month (ref. Non-IDU/Never)						2.53*	2.19
						(1.28-4.99)	(0.99-4.84)
Ever had sexual intercourse (ref. No)	2.52		2.72	2.57			
	(0.40-15.96)		(0.43-17.20)	(0.41-16.26)			
Had sexual intercourse in the last 12 months (ref. No/Never had sex)		3.77*					
		(1.19-11.97)					
Had sexual intercourse with regular partner in the last 12 months (ref. No/Never had sex)					1.24		
					(0.57-2.70)		
Had sexual intercourse with commercial partner in the last 12 months (ref. No/Never had sex)					2.20*		
					(1.09-4.48)		
Had sexual intercourse with non-regular non-commercial partner in the last 12 months (ref. No/Never had sex)					2.49*		
					(1.25-4.95)		
Frequency of condom use in the last 12 months with all regular partner(s)[a]							
Always/Often						1.15	1.13
						(0.45-2.93)	(0.40-3.20)
Sometimes/Never						1.33	1.19
						(0.57-3.11)	(0.47-3.04)
Frequency of condom use in the last 12 months with all commercial partner(s)[a]							
Always/Often						3.35*	3.41*
						(1.47-7.61)	(1.39-8.40)
Sometimes/Never						1.45	1.66
						(0.63-3.35)	(0.67-4.08)

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Table 3 Multivariate association of behavioural factors with HIV infection among female drug users in the Kathmandu Valley, Nepal *(Continued)*

Frequency of condom use in the last 12 months with all non-regular non-commercial partner(s)[a]		
Always/Often	1.71	2.13
	(0.72-4.07)	(0.82-5.53)
Sometimes/Never	3.11*	3.11*
	(1.36-7.13)	(1.28-7.56)

IDUs, injecting drug users.
[a]ref. Never had sex/No sex with this type of sexual partner in the last 12 months.
*p value <0.05.

now one of the most vulnerable populations with regard to HIV infection in Nepal.

Consistent with previous studies, injection behaviour showed a strong association with HIV infection in this population. This association could be causal because the sharing of injection instruments was associated strongly with HIV infection and in a dose-dependent manner. A study in Montreal among active drug users found that increasing injection frequency is highly correlated with HIV transmission, as it may reduce the chances of sterile injecting equipment being used each time [32]. Also, where group injecting is common, women may be the last to use the needles/syringes [33]; this may have strong implications with regard to the spread of HIV.

Unprotected sexual behaviour was also of great risk in this study. Risk significantly increased for sex with commercial or casual sex partners. The association of HIV infection and sex with commercial partners was not dose-dependent, where the people who reported more condom use were more likely to be HIV positive. The reason for this association could be multiple. It may be that participants who were involved in commercial sex and knew their HIV infection before the study might have provided socially desirable answers to our interview, or they were really using condoms to either prevent HIV transmission to their clients or as self-protection from re-infection. A recent study by UNODC among female drug users in Nepal has reported nearly 90% of condom use in last sex act with commercial sex partners [34]. In addition, previous studies among drug users have found safer sex practices strongly associated with HIV infection. A study in the United States found that self-reporting of being HIV-infected was the strongest factor associated with consistent condom use in the past 6 months [35]. Another study in Puerto Rico found that HIV-positive drug users were nearly five times more likely to use condoms during vaginal sex [36]. In contrast, HIV infection risk of the sex with casual partners was dose-dependent on condom use, where the people who have less condom use are more likely to be HIV positive. Studies in other countries have observed the association between sex with casual partners

and HIV infection among IDUs [37]. These women may not have skills to negotiate for condom use, and even if the woman is aware of her HIV status, in casual relationships she may not feel responsible for preventing further transmission of HIV to this type of partner.

Injection or sexual behaviours at high risk of HIV infection were shared by around 70% or more participants with HIV infection and even one third to half of participants without HIV infection in this study. This strongly suggests that if left uncontrolled the HIV epidemic could expand in this population and that this population could continue to be a source of HIV infection through its networks of injection and/or behavioural practices.

It is increasingly being recognized that women who use drugs are generally different from men who use drugs, and thus have different needs [6,38-40]. Targeted HIV prevention and treatment programmes should be urgently developed and implemented for this population. Provision of clean needles and syringes or methadone maintenance therapy (MMT) will be useful for the prevention of HIV transmission through injecting network. Several studies have shown that drug users who used needle and syringe exchange programs were less likely to share needles and syringes [41,42]. Programs such as needle and syringe exchange and MMT can achieve high coverage of IDUs in some settings [42]. A study in Amsterdam showed the benefits of the combined availability of needle exchange and MMT, and argued that involvement with both services, compared to only one, was associated with a lower incidence of HIV infections among IDUs [43]. Additionally, free STI diagnosis and treatment and condom distribution will be suitable for the prevention of HIV infection through sexual network [44]. Despite mixed evidence from three large community-based randomized controlled trials in sub-Saharan Africa, syndromic and mass treatment of STIs may contribute to HIV infection prevention [44]. Finally, problems of drug use and commercial/casual sex are frequently intertwined in female drug users as they often engage in commercial/casual sex to get drugs or money [45,46]. An overlap of sex and drug networks among IDUs enhances their vulnerability to HIV infection

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and promotes HIV transmission among their sexual partners. MMT, the most widely available treatment for opiate addiction, is of particular importance since it can prevent infection through both injecting drug use and commercial/ casual sex for drugs at the same time. MMT has shown to reduce both injection drug use and the risk of infection with HIV [47,48]. Since the size of this subpopulation has been unknown, these measures should be accompanied with studies to estimate the size of this population.

In this study, most of the behavioural questions were taken from the standard questions of Family Health International [27]. In this set of questions drug use and sexual behaviours are asked, though in part covering the participant's lifetime, but mostly in different time frames; one month and one year for drug use and sexual behaviours, respectively. Since such a difference in time frames could influence the predictive power of the variables, we compared their predictive powers and found that predictive powers were largely independent of time frame for both types of behaviours, suggesting that once initiated, the same behavioural pattern will be maintained over a long period of time in this population.

Older age and having education remained as strong predictors of HIV infection even in the presence of all behavioural variables that could affect HIV infection. Since HIV infection other than through injecting drug use and sexual intercourse is unlikely in this population, this may suggest the uncertainty of behavioural variables or that the behavioural variables we used could reflect the risk for HIV infection only partially. The uncertainty of information could come from self-reported nature of the information which could be affected by recall bias, the psychotic effect of drugs or by socially desirable answers to the sensitive and/or illegal behaviours.

One of the limitations of this study is the sampling procedure because it was not random; the participants may not be a true representative to the female drug user population in the study region. Participants were recruited through a snowballing process. Though efforts were made to recruit the initial respondents in many locations and opportunities to ensure variability, our sampling procedure could still introduce the bias into the participants in a way that people who have larger social connections and have similar characteristics to initial respondents are overrepresented. To get an unbiased prevalence of HIV infection and risky behaviours, more sophisticated sampling methods, such as respondent driven sampling [49-51] should be considered. Finally, cross-sectional design of this study limits the causal inference in association detected in this study.

Conclusions

HIV was highly prevalent among female drug users in Kathmandu Valley, with its risk being strongly associated not only with unsafe injection practice but also with unsafe sexual behaviours. Awareness raising programmes and preventive measures such as condom distribution, needle or syringe exchange or methadone maintenance therapy should be urgently introduced in this neglected subpopulation.

Abbreviations
IDUs: Injecting drug users; DICs: Drop-in centres; ID: Identification; STIs: Sexually transmitted infections; OR: Odds ratio; CI: Confidence interval; AOR: Adjusted odds ratio; IBSS: Integrated bio-behavioural surveillance survey; NCASC: National Center for AIDS and STD Control; MMT: Methadone maintenance therapy.

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"If I have nothing to eat, I get angry and push the pills bottle away from me": A qualitative study of patient determinants of adherence to antiretroviral therapy in the Democratic Republic of Congo

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The global response to the HIV/AIDS epidemic has improved access to antiretroviral therapy (ART) and has contributed to decreased HIV/AIDS morbidity and mortality in sub-Saharan Africa. Patient adherence to ART is crucial to the success of HIV/AIDS treatment. However, little is known about the determinants of adherence to ART among people living with HIV/AIDS (PLWHA) in the Democratic Republic of Congo (DRC). This qualitative study used in-depth semi-structured patient interviews, a purposive sampling strategy and thematic analysis scheme to identify barriers and facilitators of adherence to ART in the DRC. We recruited three categories of participants from the Centre Hospitalier Monkole and the NGO ACS/Amo-Congo including participants on antiretroviral (ARV) treatment (*n* = 19), on ARV re-treatment (*n* = 13) and lost to follow-up (*n* = 6). Among 38 participants interviewed, 24 were female and the median age was 41 years. Food insecurity as a barrier to adherence emerged as a dominant theme across the three categories of participants. Other barriers included financial constraints, forgetfulness and fear of disclosure/stigma. Religious beliefs were both a barrier and a facilitator to ART adherence. We found that food insecurity was a common and an important barrier to ART adherence among patients in the DRC. Our findings suggest that food insecurity should be appropriately addressed and incorporated into ARV treatment programs to ensure patient adherence and ultimately the long-term success of HIV treatment in the region.

Keywords: ART; adherence; food insecurity; AIDS; Democratic Republic of Congo

Introduction

Access to antiretroviral therapy (ART) in sub-Saharan Africa has improved considerably over the past several years and has contributed to decreased HIV/AIDS morbidity and mortality in the region (Brinkhof et al., 2009; Mills et al., 2011; UNAIDS, 2012). However, in addition to treatment access, high and sustained patient adherence to ART is sine qua non for maximizing both its therapeutic and preventive benefits (Kalichman et al., 2010; Paterson et al., 2000).

Prior studies have documented a number of determinants of adherence to ART, ranging from economic and structural to sociocultural factors, as well as factors such as the complexity of the regimen, side effects; forgetfulness and inadequate knowledge (Badahdah & Pedersen, 2011; Balcha, Jeppsson, & Bekele, 2011; Curioso, Kepka, Cabello, Segura, & Kurth, 2010; Hardon et al., 2007; Mills et al., 2006; Mshana et al., 2006; Tsai & Bangsberg, 2011; Tuller et al., 2009; Wanyama et al., 2007). However, there are still important research gaps which need to be addressed.

Previous studies have not examined adherence to ART among patients with different treatment profiles; this approach might allow new insights into factors that constrain and facilitate ART adherence. In addition, there is a very limited literature on ART adherence in Democratic Republic of Congo (DRC) which remarkably restricts our understanding of factors associated with ART adherence, and renders studies on ART adherence in the DRC a research priority.

This qualitative study expands on the current available knowledge and address the above cited research gaps by exploring barriers and facilitators of adherence to ART in three different groups of participants including those on ART with no history of treatment interruption, on ART with history of treatment interruption and those lost to follow-up in the DRC's sociocultural context.

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Methods

Participants

The study was conducted in Kinshasa, the DRC in March 2011. Participants were recruited from two health facilities, the Centre Hospitalier Monkole (CHM) and the NGO Actions Communautaires Sida/Avenir Meilleur pour les Orphelins (ACS/Amo-Congo) through a maximum variation, purposive sampling strategy (Bowers, House, & Owen, 2011). Our participants consisted of (1) participants who successfully completed at least six months of treatment since antiretroviral (ARV) treatment initiation, herein referred as participants *on ARV treatment*, (2) participants who were on ARV re-treatment after at least one month of ART interruption, referred to as participants *on ARV re-treatment*, and (3) participants who were *lost to follow-up*. We considered as lost to follow-up, participants who were unable to show up for ARV refills for three consecutive months (90 days) after the date of the last medical appointment. To be eligible for inclusion in the study, participants had to be at least 18 years old, HIV positive, and belong to one of the aforementioned categories. Subjects were recruited when they attended the health centers for routine medical examination or when refilling their monthly ART prescription. Participants from the lost to follow-up group were recruited through phone calls made to mobile numbers that were available on their medical files. The research team conducted additional outreach to patients lost to follow-up who could not be reached through phone calls, using addresses from medical files. Upon explaining the purpose of the study and assuring strict confidentiality, all participants provided written informed consent and completed a questionnaire on sociodemographic characteristics prior to conducting interviews. Participants were compensated for their time and transportation with an amount of 10 US dollars. This study was granted ethical approval from the Committee for Research on Human Subjects at Kyoto University and the Kinshasa School of Public Health Ethics Review Committee in the DRC.

Data collection and analysis

A literature review of ART adherence informed the development of a semi-structured interview guide. The interview guide was designed to explore topics related to participants' experiences, beliefs, behaviors, opinions, and knowledge about HIV/AIDS and ART. Probes were used to gain detailed insights and facilitate emergence of new themes. Specific questions explored reasons for medication interruption, cues to restart ART among participants on ARV re-treatment and reasons for dropping out and barriers to restarting ART among patients lost to follow-up. A preliminary insight of data were obtained through debriefing sessions conducted at the end of each interview to note the main emerging themes and to plan how to address those themes more effectively in subsequent interviews. Interviews lasted from 25 minutes to 1 hour and were conducted in French and Lingala, the most commonly used languages in Kinshasa.

Interviews were digitally recorded, then transcribed verbatim and translated into English. All the transcripts were reviewed for accuracy by comparing with the recordings. Field notes and data-set transcripts constituted the final material for analysis. Data were manually analyzed using a thematic-analysis approach. This approach involves getting familiarized with the data through an iterative process of reading the data-set transcripts, generating initial codes, arranging codes into larger categories, drawing connections between codes and categories until generation of a saturated thematic map of the analysis (Braun & Clarke, 2006). The analytical process included a separate data analysis of participants on ARV treatment, re-treatment and, lost to follow-up, allowing new insights into determinants of ART adherence across the three categories of participants. Initially, two investigators (PMM & TT) independently coded the transcripts and identified emerging themes relevant to the research question. Discrepancies in coding were discussed and resolved by consensus and codes were organized into larger categories. In the second phase, codes, and categories were revised and refined through regular meetings with an expert panel (MDF, MOK & MK). Quotes from the participants are provided in support of the themes we identified and are lightly edited for ease of reading. Efforts were made to not substantially alter the contents of the quotes.

Results

Description of study participants

Thirty-eight participants were interviewed, considering the sample size of 5–25 participants potentially needed to achieve thematic saturation from previous studies (Creswell, 2007). Nineteen participants (50%) were currently on ARV treatment, 13 (34%) on ARV re-treatment, and 6 (16%) were lost to follow-up. The median age of participants was 41 years; most had completed primary education but were without standard employment and had a monthly income of less

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than 20 US dollars. Almost half reported having irregular meals (Table 1).

Barriers to adherence

We found an overall similarity in the pattern of themes that emerged across the three categories of participants (Table 2).

Food insecurity

Food insecurity was the most common theme that emerged both as a day-to-day barrier to ART adherence among participants from ARV treatment and re-treatment group and as one of the principal reasons for ART interruption among participants from the ARV re-treatment and lost to follow-up group. Participants described two pathways through which food insecurity constrained adherence to ART: (1) experiencing increased ART side effects and (2) the belief that ART does not work or is harmful when taken without food. Several participants reported experiencing uncomfortable side effects when they took her medication on an empty stomach. One participant said:

Table 1. Sample characteristics.

Variable	$N = 38$	%
Age in years (median) 41		
Gender		
Male	14	36.8
Female	24	63.2
Marital status		
Single, separated	13	34.2
Married, cohabitating	21	55.3
Widow/widower	4	10.5
Treatment category		
On ARV treatment	19	50.0
On ARV re-treatment	13	35.2
Lost to follow-up	6	15.8
Education level		
None	2	5.3
Primary	8	21.1
Secondary	20	52.6
University	8	21.1
Profession		
With employment	13	34.2
Without employment	25	65.8
Monthly income		
< 20$	17	44.7
20–100$	17	44.7
> 100$	4	10.5
Meal/day		
Regular ($\geq$ 2 meals)	22	57.9
Irregular ($\leq$ 1 meal)	16	42.1

Table 2. Summary of themes by treatment category.

Themes	Treatment category		
	On ARV treatment	On ARV re-treatment	Lost to follow-up
Food insecurity	✓ −	✓ −	✓ −
Financial insecurity	✓ −	✓ −	✓ −
Forgetfulness	✓ −	✓ −	✓ −
Fear of disclosure/ stigma	✓ −	✓ −	✓ −
Religious beliefs	✓ +	✓ ±	✓ −
Others			
Travel/ migration		✓ −	✓ −
Feeling hopeless		✓ −	✓ −
Side effects	✓ −	✓ −	✓ −
Alcohol	✓ −	✓ −	✓ −
Traditional medicines		✓ −	✓ −

✓indicates in rank order the themes that emerged and affected ART adherence.
− indicates a barrier of adherence to ART.
+ indicates a facilitator of adherence to ART.

> It's very tough to take the pills when there is nothing to eat. I made two weeks I was not taking the pills. When I took them without food I had stomach aches. (41-year-old female on ARV treatment)

The belief that the medicines are not effective or harmful when taken on an empty stomach also affected adherence to ART:

> The only problem is just about eating. You need to eat for this treatment to work. If I have no food I don't take pills. Like today I didn't take my pills because I couldn't eat (35-year-old female on ARV re-treatment)

> The medication can be good but can also be bad for the body if you take them without foods. Taking pills without eating can actually cause much damage in your body. (63-year-old male lost to follow-up)

Food insecurity was a daily concern and a source of frustration for participants and their family members. As one participant stated:

> I really have financial problems; I don't know what to do. Sometimes I am just fed up, mainly if I have nothing to eat, I get angry and push the pills bottle away from me. (45-year-old female on treatment)

Financial insecurity

Another important theme that impacted adherence was financial insecurity. Participants expressed

difficulty securing money for transportation to attend clinical visits or other medical-related expenses such as medical tests or clinical examination fees. This resulted in some of them missing their medication refill appointments or temporarily interrupting their medication. Moreover, we noted that other medical-related expenses constituted a barrier to restarting ART among patients lost to follow-up. Although both health facilities offered ART free of charge, participants still had to pay for other ancillary costs. For example, a 48-year-old male participant who interrupted ART after relocating in the hinterland of Congo explained his difficulties in restarting the treatment when he came back to the city of Kinshasa:

> I was discouraged when I learned from somebody that there (meaning the health facility) they ask 25$ for the CD4 test. I was really trying to figure out how to take contact with the health facility for restarting my treatment until when you contacted me. (48-year-old male lost to follow-up)

Participants sometimes had to balance between allocating their very limited budget on either their medical expenses or on household needs such as paying for children' education or securing food for the household. One participant said:

> At a certain time I stopped taking my medication because I had many financial problems, I had to take care of children's education and moreover you need to eat when you take those pills. (48-year-old male on ARV re-treatment)

Forgetfulness

Forgetfulness was a common reason for skipping doses among participants from all the categories. In a few instances, forgetfulness resulted in taking more than the prescribed dose. One participant said:

> Sometimes, it happens that I forget that I have already taken my evening pills; in that case I will take another one just to be sure I don't miss. I notice that when I run out of pills before the next appointment for treatment refill and then I just remember that I took more than two doses the other day. (44-year-old male on ARV treatment)

Fear of disclosure/stigma

Participants often did not disclose their HIV status out of fear of rejection and gossip. Some participants pointed to stigma as a potential barrier to ART adherence; however, this did not affect adherence inasmuch as most of them used coping strategies such as taking pills secretly or faking the name of pills when asked. In contrast, a number of participants admitted to interrupting their medication out of fear of inadvertently disclosing their HIV status. One participant said:

> I was not here (meaning that she was not at home). I went to live at my grandparents' place; over there they were not aware of my disease, so I didn't want them to know. (28-year-old female on ARV re-treatment)

Religious and traditional beliefs

Religious beliefs were both a barrier and a facilitator of ART adherence. The belief that one's disease was caused by witchcraft led a few participants from the ARV re-treatment and lost to follow-up groups to interrupt their medication and to use prayers and/or traditional medicines in search for potential cure. On the other hand, many participants sustained the belief that it is God who provided the knowledge to make ARVs; this mindset motivated them to keep adhering to the treatment:

> I am a Christian and a believer, I know that God exists but those medicines also were inspired by God. God is the one who gave inspiration to doctors to make those medicines for us. (59-year-old male on ARV treatment)

> Those medicines just give you strength but God is the one who cures. Because it is God who gave you intelligence to find out medicines, so through medicines I can get cured; before putting the pills in your mouth you must have faith. (37-year-old female on ARV re-treatment)

Other barriers

Other reported barriers included travel or migration, feeling hopeless, side effects, and the use of traditional medicines. Other participants reported delaying or skipping ART doses after alcohol consumption.

Discussion

This is the first qualitative study to examine ART adherence correlates among HIV-positive people with different treatment experiences, and the first to examine adherence among HIV-infected adults in Kinshasa, DRC. We found that food insecurity was the most frequently reported barrier to ART adherence among our participants. Previous studies on ART adherence have identified food insecurity as a contributing factor of nonadherence to ART, but none of these prior studies examined barriers to ART adherence among participants with different treatment experiences (Hardon et al., 2007; Nagata et al.,

2012; Sanjobo, Frich, & Fretheim, 2008; Weiser et al., 2010). Our study purposively selected participants with different treatment profiles, namely participants who were on ARV treatment, re-treatment, and lost to follow-up. Examining adherence barriers exclusively with participants on ARV may reveal only a partial picture of barriers to ART adherence; since this group represents participants who have so far managed to adhere to treatment so, barriers identified essentially reflect those that interfere with day-to-day ART adherence. Thus, knowledge on these two last patients groups is vital as poor adherence and ART interruption foster emergence of HIV drug resistance, which, besides affecting long-term effectiveness of ART at the individual level, raises serious public health implications with potential transmission of drug-resistant strains of HIV (Danel et al., 2009; Gupta et al., 2012; Lima et al., 2008; Luebbert et al., 2012).

Participants reported skipping ART doses in the absence of food; this held true for participants in the ARV treatment and re-treatment groups. In addition, participants in the ARV re-treatment and lost to follow-up groups identified food insecurity among the main reasons for their treatment interruption.

Food insecurity is associated with a number of adverse health behaviors. For instance, a previous study found increased risky sexual behaviors among food-insecure women in Botswana and Swaziland (Weiser et al., 2007). Moreover, food insecurity was shown to be associated with unsuppressed viral load which may lead to treatment failure (Wang et al., 2011). These findings suggest that effective strategies to promote food access to patients on ART should be implemented in order to curtail the negative effects of food insecurity on ART adherence in the DRC. For example, nutritional support to food-insecure patients was shown to improve both ART adherence and patient retention in care in sub-Saharan Africa (Cantrell et al., 2008).

Additionally, addressing financial constraints is also critically important in improving adherence to ART. These results are in line with a recent study in Mozambique which showed that adherence to ART and patient retention in care improved when patients were organized in small groups, and collected pills for all the members on a rotating basis to reduce the cost of transportation (Decroo et al., 2010).

We also found that stigma and fear of disclosure were barriers to ART adherence. Most participants kept their HIV status secret and revealed it only in a very restricted social network such as the immediate family. Although patients listed stigma and fear of disclosure as a barrier to ART adherence, this did not seem to decrease their actual adherence since many of them used strategies such as disguising or taking their medication secretly to avoid disclosure. However, such strategies were more difficult to sustain over long periods of time in an environment which they considered hostile for disclosure; for example, when patients relocated to a relative's home, then resolved to interrupt medication to avoid unintentional disclosure.

We found that religious beliefs were both a barrier and facilitator of ART adherence. Previous studies have identified beliefs in spiritual healing and/or beliefs around the causes of HIV to impact negatively on ART adherence (Mshana et al., 2006; Roura et al., 2009; Wanyama et al., 2007). Participants who believed their disease was caused by witchcraft interrupted their medication to seek healing through prayers and/or traditional medicine. Conversely, some patients thought of ART as an expression of God's knowledge transmitted to care providers, and this was sufficient incentive for them to stick with medication. These findings fit with the social context of the DRC where religious and spiritual beliefs are essential components of people's lives (Maman, Cathcart, Burkhardt, Omba, & Behets, 2009). Addressing religious barriers in interventions designed to promote adherence to ART in such settings might help to improve patient retention in ART programs. Faith-based organizations can positively impact on ART adherence by promoting ARVs as a divine tool to fight HIV/AIDS.

Our study has some limitations. First, there might be a selection bias with participants lost to follow-up. A significant number of lost to follow-up were reported dead suggesting that those we recruited might represent a specific group of survivors with different views and experiences. Second, participants were all selected from private health facilities that supplied ARVs free of charge. It is possible that participants from the public health sector may offer another picture of barriers of adherence to ART, especially in settings where ARVs are not free. Finally, although we believe that our results may be extended to similar settings; it is unclear to what extent they can be applied in different contexts in sub-Saharan Africa.

However, this study is unique in that it captures diverse perspectives of determinants of adherence to ART from participants with different treatment profiles. In addition, we found that in response to the same adherence barrier, participants adopted different medication taking behavioral trajectories namely the interruption or just skipping a daily dose of their medication. Furthermore, it would not have been possible to unveil the negative impact of religious beliefs, travel/migration, feeling hopeless, and traditional medicines on ART adherence if we

examined adherence only with participants in the ARV treatment group.

Conclusion

We found that food insecurity emerged as a common and an important barrier to ART adherence among patients in the DRC. HIV treatment and care programs should comprehensively address food insecurity in the context of other sociocultural-related factors to ensure patient adherence to ART and ultimately long-term success of HIV treatment in the region.

Acknowledgements

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Food Insecurity Is Associated with Increased Risk of Non-Adherence to Antiretroviral Therapy among HIV-Infected Adults in the Democratic Republic of Congo: A Cross-Sectional Study

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Abstract

Background: Food insecurity is increasingly reported as an important barrier of patient adherence to antiretroviral therapy (ART) in both resource-poor and rich settings. However, unlike in resource rich-settings, very few quantitative studies to date have investigated the association of food insecurity with patient adherence to ART in Sub-Saharan Africa. The current study examines the association between food insecurity and adherence to ART among HIV-infected adults in the Democratic Republic of Congo (DRC).

Methods and Findings: This is a cross-sectional quantitative study of patients receiving ART at three private and one public health facilities in Kinshasa, DRC. Participants were consecutively recruited into the study between April and November 2012. Adherence was measured using a combined method coupling pharmacy refill and self-reported adherence. Food insecurity was the primary predictor, and was assessed using the Household Food Insecurity Access Scale (HFIAS). Of the 898 participants recruited into the study, 512 (57%) were food insecure, and 188 (20.9%) were not adherent to ART. Food insecurity was significantly associated with non-adherence to ART (AOR, 2.06; CI, 1.38–3.09). We also found that perceived harmfulness of ART and psychological distress were associated respectively with increased (AOR, 1.95; CI, 1.15–3.32) and decreased (AOR, 0.31; CI, 0.11–0.83) odds of non-adherence to ART.

Conclusion: Food insecurity is prevalent and a significant risk factor for non-adherence to ART among HIV-infected individuals in the DRC. Our findings highlight the urgent need for strategies to improve food access among HIV-infected on ART in order to ensure patient adherence to ART and ultimately the long-term success of HIV treatment in Sub-Saharan Africa.

Introduction

The benefits of antiretroviral therapy (ART) in reducing HIV/AIDS related-morbidity and mortality are extensively documented [1–3]. Recent evidence indicates that early initiation of ART substantially reduces sexual transmission of HIV at individual [4,5] and population levels [6]; conferring ART a crucial place in both treatment and prevention of HIV/AIDS.

Prior studies have shown that, without high and sustained adherence levels, both therapeutic and public health benefits of ART cannot be secured, and that individuals with sub-optimal levels of adherence have higher risk of incomplete viral suppression, disease progression, and development of drug resistance [7–9].

Our understanding of adherence to ART has substantially increased over the past years with a wide documented range of factors influencing ART adherence across differing settings in developed and developing countries [10–17]. Recently, food insecurity has emerged as a key structural barrier that affects adherence to ART in both resource-rich and constrained settings. Studies from British Columbia [18], San Francisco [19], Atlanta [20,21], and France [22] have found lower levels of medication adherence among food insecure individuals on ART. Similarly, a number of, predominantly qualitative, studies from Sub-Saharan

Africa (SSA) have documented food insecurity as an important barrier to ART adherence [12,23–26]. Furthermore, food insecurity was shown to be independently related to poor virologic response and mortality even when adjusting for patient adherence to ART [19,27,28].

Food insecurity parallels, and is viciously intertwined with the AIDS epidemic in SSA, both having a damaging impact in the region [29]. SSA accounts for 69% of the people infected with HIV worldwide, and is home to 234 million (26.8%) people classified as undernourished [1,30]. In the Democratic Republic of Congo (DRC), the research setting of the current study, the Multi Indicator Cluster Survey (MICS) revealed that approximately 33% of the households were experiencing food insecurity in 2010, with figures ranging from 5% in the Kinshasa City to nearly 60% in some eastern provinces of the DRC [31]. The national HIV program reports a HIV prevalence of 2.57% among the general population, with only 12.3% of eligible patients having access to ART [32].

A review of the literature revealed that, unlike in resource-rich settings, very few quantitative studies to date, using a validated measure of food insecurity, have documented the association between food insecurity and patient adherence to ART in SSA and the developing world at large [26,33]. Additionally, literature on patient adherence to ART in the DRC, the second largest country in Africa, remains exceptionally scarce. In our preliminary qualitative study, we found that food insecurity, financial constraints, forgetfulness, and fear of disclosure/stigma were common barriers to ART adherence; while religious beliefs were both a barrier and facilitator of ART adherence among HIV-positive adults in the DRC [23].

The current study, grounded in the results of our qualitative study [23], aims at quantitatively assessing factors associated with adherence and more specifically, documenting the prevalence of food insecurity, and its effect on ART adherence among HIV-positive adults receiving ART in the DRC. Such information is crucial for guiding context-specific interventions to promote patient adherence to ART.

Methods

Ethics Statement

This study was granted ethical approval from the Committee for Research on Human Subjects at Kyoto University and the Kinshasa University School of Public Health Ethics Review Committee in the DRC. All the participants provided written informed consents before being interviewed.

Study Design, Participants and Setting

This is a cross-sectional study conducted in Kinshasa, DRC, between April and November 2012. Participants were consecutively recruited into the study from one public health facility: Hopital Provincial General de Référence de Kinshasa (HGPRK) and three private health institutions which included one treatment site of the NGO Actions Communautaires Sida/Avenir Meilleur pour les Orphelins (ACS/Amo-Congo), three treatment sites of the Armée du salut (Salvation Army), and two treatment sites of the Centre Hospitalier Monkole (CHM). Recruitment sites were in geographically dispersed locations and served patients coming from all the townships of Kinshasa. At the time the study was conducted, around 1,000, 2,900, 2,300, and 1,100 patients were receiving free ART respectively at the HGPRK, ACS/Amo-Congo, Armée du salut, and the CHM, and none of the facilities provided food or any kind of nutrition aid to patients. We collected data using an interviewer-administered questionnaire, which we designed based on the findings from our prior qualitative study [23] supplemented with other relevant questions obtained from the available literature [34–38]. The questionnaire was piloted in a sample of 20 respondents (not included in the final sample) to ensure clarity prior to conducting interviews, and it showed an overall good test-retest reliability performed within a one month interval. The interviews were conducted in French or Lingala, the most commonly used languages in Kinshasa, and the interviewers were provided guidance on questionnaire administration over two training sessions organized by the research team. Participants were included in the study provided that they were at least 18 years old, on ART for at least 6 months, and had given written informed consent. Participants were compensated for their time and transportation with an amount of 3 US dollars.

Measures

Primary outcome. The primary outcome of interest was adherence to ART, and was assessed using a composite measure coupling both pharmacy refill and self-reported adherence. Pharmacy refill adherence measures were shown to be reliable in assessing adherence, and to correlate well with virological and clinical outcomes in resource limited settings [39–42], and the combination with self-reported adherence performed better in predicting virological failure than other singular methods [43].

The pharmacy refill adherence in this study is based on a variation of the medication possession ratio (MPR), a measure of the proportion of days a patient has his/her medication on hand, and was calculated by dividing the number of days late for pharmacy refills by the total days on ART, and then subtracting this proportion from 100% [40,44]. We calculated the average pharmacy refill rate of adherence for each patient over the preceding six months. When applicable, the number of days being late for pharmacy refills was adjusted to account for cases where patients were provided with more medication than needed. Patients with pharmacy adherence levels <95% were categorized as non-adherent to ART [8].

To measure self-reported adherence, we adopted a validated tool that assesses adherence over the previous seven days [34]. The tool contains questions that first measure adherence over shorter time frames (yesterday and the day before yesterday), and an aided-recall question for situations that can potentially lead to missed ART doses with the intent to facilitate a more accurate reporting of the number of pills skipped during the previous seven days, and to limit the influence of forgetfulness. Self-reported non-adherence was defined as taking <95% of the prescribed pills over the previous seven days [8].

In this study, participants were categorized as non-adherent to ART when they were non-adherent to either one or both of the measures of adherence described above; otherwise, they were considered to be adherent.

Primary independent variable. Food insecurity was the primary independent variable of this study, and was measured by the Household Food Insecurity Access Scale (HFIAS) [35]. The HFIAS is a validated instrument and has been shown to distinguish food insecure from food secure households across different cultural contexts. It is a set of nine questions designed to reflect universal domains of the experience of food insecurity including 1) anxiety and uncertainty about the household food supply, 2) insufficient quality (includes variety and preferences of the type of food), and 3) insufficient food intake and its physical consequences. We presented results in a categorical format including 1) food secure, 2) mildly food insecure 3) moderately food insecure, and 4) severely food insecure, which we dichotomized into food insecure versus food secure. The Cronbach's

alpha was 0.97, demonstrating a high internal consistency of the scale in our sample.

Other covariates. *Internalized AIDS stigma*: The Internalized AIDS-Related Stigma Scale was used to assess the internalized AIDS stigma [36]. The items were administered on a 5-point Likert-scale ranging from strongly disagree to strongly agree. Strongly disagree, disagree, and neutral were converted to 0 and agree and strongly agree to 1. Scale score ranged 0–6; participants who obtained relatively high scores on the scale (>2) were compared to those who had low scores (≤2) [45]. The scale showed a moderate degree of internal consistency with Cronbach's alpha = 0.60.

Psychological distress (Depression, anxiety disorders): Mental health status was assessed using the Kessler-6 scale, a standardized and validated screening tool for non-specific psychological distress including depression and anxiety disorders [37]. Participants were asked on a 5-points Likert scale ranging from 0 (none of the time) to 4 (all of the time) how often they felt 1) nervous, 2) hopeless, 3) restless or fidgety, 4) so depressed that nothing could cheer you up, 5) that everything was an effort, and 6) worthless. Scores equal to or higher than 13 indicate higher probability of psychological distress. There was a high internal consistency of the scale in our sample with Cronbach's alpha = 0.89.

Other variables: other covariates included the household wealth index [46], socio-demographic characteristics (10 items), HIV/AIDS disease-related variables (4 items) and HIV/AIDS knowledge (8 items), ART-related variables (8 items), perceptions about HIV/AIDS and ART (12 items), alcohol and drug use (2 items), social support [47], and perceived quality of health care (6 items) [38]. (See Text S1 for additional information on variables).

Statistical Analysis

Data was analyzed using SPSS (PASW) for Windows 17.0 (SPSS Inc., Chicago, Illinoi, USA). Univariate analysis was conducted to obtain descriptive statistics of all the variables. Bivariate analyses were performed using Chi-square tests for categorical variables and Mann Whitney U-test for continuous variables. We included in the analysis nonresponse cases on items related to perceptions about HIV/AIDS and ART; their exclusion did not affect the results of our analysis (See Table S1, which shows frequency of nonresponse for perception items). We grouped nonresponses with participants whose answers were "disagree" and "don't know" since they were similar with respect to their odds ratios when compared to participants who agreed to the assertions. Factors associated with non-adherence by bivariate analysis with P value ≤0.10 and those considered epidemiologically important were entered into a multivariate logistic regression model to obtain adjusted odds ratios (AOR) and 95% confidence intervals (CI). "Frequency of ART" and "regimen drugs" were not included in the multivariate model, even though both variables had each a category with P value ≤0.10, overall the two variables did not meet the inclusion criteria, and we excluded "duration of HIV infection" from the model because of its multicollinearity with "duration of ART".

Results

Participant Characteristics

A total of 898 participants completed the study and 25 declined participation, giving a response rate of 97.3%. The median age was 44 years [Interquartile range (IQR): 38–51]. The majority of participants were female (72.2%), without standard employment (76.4%), had completed at least secondary school (75.3%), and

Christians (87.9%) by religion (Table 1). The median treatment duration was 41 months (IQR: 18–64); most participants were on first line regimens (97.9%), and on a twice a day dosing schedule (92.3%). (Table 2).

Food Insecurity and Adherence Assessment

Based on the HFIAS, 386 participants (43.0%) were classified as food secure, 9 (1.0%) as mildly food insecure, 46 (5.1%) as moderately food insecure and 457 (50.9%) as severely food insecure (See Table S2, which shows details of participants' food security status). The overall prevalence of food insecurity among our participants was 57% (Table 2). 188 (20.9%) participants were categorized as non-adherent to ART in respect to the definition of adherence described above (See Table S3, which shows details of participants' adherence status).

Bivariate Associations between Independent Variables and ART Adherence

Factors significantly associated with non-adherence in the bivariate analysis included food insecurity [odds ratio (OR), 2.25; CI, 1.58–3.19; P = 0.000)], psychological distress (OR, 0.38; CI, 0.15–0.98; P = 0.039), presence of (an)other HIV-infected individual(s) in the household (OR, 0.62; CI, 0.40–0.96; P = 0.042), alcohol intake (OR, 1.65; CI, 1.13–2.40; P = 0.012), duration of ART [≥48 months] (OR, 1.45; CI, 1.05–2.01; P = 0.027), perceived ART harmfulness (OR, 1.68; CI, 1.10–2.55; P = 0.042), and the beliefs that God or prayers could cure HIV (OR, 2.10; CI, 1.45–3.04; P = 0.000), or that ART worked better when associated with prayers (OR, 1.73; CI, 1.23–2.43; P = 0.002), and receiving treatment from ACS/Amo-Congo (OR, 2.99; CI, 1.58–5.62; P = 0.001). (Table 2 & Table 3).

Table 4 shows reasons reported by participants for skipping ART doses during the previous seven days. 36 (39.5%) participants cited forgetfulness, 17 (18.6%) were unable to pay for the medical consultation or for transport, 13 (14.2%) ran out of pills, 11 (12.0%) reported lack of food, 7 (7.6%) had travelled, and other reasons were reported in much lower proportions.

Multivariate Analysis

In the multivariate analysis (Table 5), food insecurity was strongly associated with non-adherence. Food insecure participants were two times more likely to be non-adherent to ART compared to those who were food secure (AOR, 1.99; CI, 1.36–2.90, P = 0.000). Other factors significantly associated with non-adherence to ART included alcohol intake (AOR, 1.55; CI, 1.02–2.34, P = 0.037), and perceived ART harmfulness (AOR, 2.06; CI, 1.30–3.27, P = 0.002). Paradoxically, we found that participants who had psychological distress (depression, anxiety) as measured by the K6-scale, had lower odds of non-adherence (AOR, 0.34; CI, 0.12–0.90, P = 0.030), as well as those who reported that skipping ART doses could worsen the disease (AOR, 0.58; CI, 0.38–0.88, P = 0.012).

Discussion

Designed based on the findings of our preceding qualitative study that food insecurity is a prominent structural barrier to ART adherence [23], this study is one of the first to quantitatively demonstrate the association of food insecurity with ART nonadherence in a Sub-Saharan African country. Our findings corroborate previous qualitative studies from SSA [12,23–25], quantitative studies in resource rich settings [18–22], and recent findings from a longitudinal cohort study in rural Uganda [26].

Table 1. Sociodemographic characteristics of non-adherent and adherent participants on ART recruited in Kinshasa, DRC.

	Non-Adherent (n = 188)	Adherent (n = 710)	Total (n = 898)	Crude OR (95% CI)	P value
	n (%)	n (%)	n (%)		
Gender					
Male	49 (26.1)	201 (28.3)	250 (27.8)	1.00	
Female	139 (73.9)	509 (71.7)	648 (72.2)	1.12 (0.77–1.61)	0.603
Educational level					
Primary school or less	46 (24.5)	176 (24.8)	222 (24.7)	1.00	
Secondary school	110 (58.5)	420 (59.2)	530 (59.0)	1.00 (0.68–1.47)	1.000
University	32 (17.0)	114 (16.0)	146 (16.3)	1.07 (0.64–1.78)	0.885
Marital status					
Married/cohabitating	63 (33.5)	261 (36.8)	324 (36.1)	1.00	
Single	43 (22.9)	164 (23.1)	207 (23.1)	1.08 (0.70–1.67)	0.793
Divorced/Separated	29 (15.4)	83 (11.7)	112 (12.5)	1.44 (0.87–2.39)	0.191
Widowed	53 (28.2)	202 (28.4)	255 (28.4)	1.08 (0.72–1.63)	0.768
Religion					
Catholic Christian	54 (28.7)	194 (27.3)	248 (27.6)	1.00	
Protestant Christian	22 (11.7)	125 (17.6)	147 (16.4)	0.63 (0.36–1.09)	0.127
Revival churches Christian	85 (45.2)	309 (43.5)	394 (43.9)	0.98 (0.67–1.45)	1.000
Others*	27 (14.4)	82 (11.5)	109 (12.1)	1.18 (0.69–2.00)	0.627
Employment status					
Employed	37 (19.7)	175 (24.6)	212 (23.6)	1.00	
Unemployed	151 (80.3)	535 (75.4)	686 (76.4)	1.33 (0.89–1.98)	0.184
IGA					
Yes	136 (72.3)	478 (67.3)	614 (68.4)	1.00	
No	52 (27.7)	232 (32.7)	284 (31.6)	0.78 (0.55–1.12)	0.220
	Median (IQR)	Median (IQR)	Median (IQR)		
Age (years)	43 (36. 25–50)	44 (38–51)	44 (38–51)		0.150
Household size	5 (4–7)	5 (3–7)	5 (3–7)		0.426
Financial dependents†	3 (1.25–5)	3 (1–5)	3 (1–5)		0.820
Household wealth index	0.08 (−2.29 to 2.55)	0.16 (−2.44 to 2.42)	0.16 (−2.43 to 2.42)		0.823

*Other: Muslim, Kimbaguist, None;
†number of financial dependents; ART, antiretroviral therapy; IGA, income generating activity; OR, odds ratio; IQR, inter-quartile range; DRC, Democratic Republic of Congo.
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Because of the cross-sectional nature of this study, interpretation of the results could be multiple. Firstly the observed association could be confounded by a third factor that was associated with both ART non-adherence and food insecurity. Secondly, we could assume that ART non-adherence was causal to food insecurity. Lastly, food insecurity could be causal to ART non-adherence.

The first possibility could be the case with poverty as a most likely confounder since prior studies have shown that trade-offs between subsistence needs and health care needs resulted in participants missing clinic visits or giving up ART for food in financially constrained individuals [24,48]. However, our results failed to support this possibility because household wealth index and employment status were not associated with ART non-adherence in bivariate analyses and our multivariate analysis was adjusted for these variables. Residual confounding of poverty due to insufficient sensitivities of these measures to rate poverty seemed unlikely because both variables were strongly associated with food insecurity (P<0.001). The second possibility seemed also unlikely because such a narrative had never been documented in qualitative studies including our study [12,23–25] and because ART non-adherence was not associated with any financial measures such as household wealth index and employment status. The third possibility is therefore most likely the case. This is strongly supported by the recent findings from a study in rural Uganda showing that food insecurity is longitudinally associated with non-adherence to ART [26] and preliminary experimental studies that showed that food supplementation improved the adherence to ART among food-insecure adults in Zambia [49,50].

However, possible mechanisms through which food insecurity could lead to ART non-adherence remained unclear. Our qualitative study identified two perceptions held by the participants as potential mechanisms including ART can be harmful or is not effective when taken without food [23]. In this study, we tested these hypotheses including the questions on participants' perception on the harmfulness or effectiveness of ART when taken without food but failed to show any association of these perceptions with ART non-adherence. Possible mechanisms may include forgetfulness. Although our study was not designed to

Table 2. Bivariate analysis of factors associated with Non-adherence to ART.

	Non-Adherent (n = 188)	Adherent (n = 710)	Total (n = 898)	Crude OR (95% CI)	p value
	n (%)	n (%)	n (%)		
Food insecurity					
No	53 (28.2)	333 (46.9)	386 (43.0)	1.00	
Yes	135 (71.8)	377 (53.1)	512 (57.0)	2.25 (1.58–3.19)	0.000
Disclosure					
No	36 (19.1)	170 (24.0)	206 (22.9)	1.00	
Yes	152 (80.9)	540 (76.0)	692 (77.1)	1.32 (0.88–1.98)	0.196
Psychological distress					
No (Score:0–12)	183 (97.3)	663 (93.4)	846 (94.2)	1.00	
Yes (Score:13–24)	5 (2.7)	47 (6.6)	52 (5.8)	0.38 (0.15–0.98)	0.039
Internalized stigma					
Score:0–2	123 (65.4)	483 (68.0)	606 (67.5)	1.00	
Score:3–6	65 (34.6)	227 (32.0)	292 (32.5)	1.12 (0.80–1.57)	0.555
Social support from family					
No	96 (51.1)	417 (58.7)	513 (57.1)	1.00	
Yes	92 (48.9)	293 (41.3)	385 (42.9)	1.36 (0.98–1.88)	0.071
Social support from non-family members					
No	137 (72.9)	544 (76.6)	681 (75.8)	1.00	
Yes	51 (27.1)	166 (23.4)	217 (24.2)	1.22 (0.84–1.75)	0.331
Opportunistic infection					
No	181 (96.3)	683 (96.2)	864 (96.2)	1.00	
Yes	7 (3.7)	27 (3.8)	34 (3.8)	0.97 (0.41–2.28)	1.000
HIV-infected individual(s) in the household					
No	160 (85.1)	554 (78.0)	714 (79.5)	1.00	
Yes	28 (14.9)	156 (22.0)	184 (20.5)	0.62 (0.40–0.96)	0.042
Alcohol intake*					
No	139 (73.9)	585 (82.4)	724 (80.6)	1.00	
Yes	49 (26.1)	125 (17.6)	174 (19.4)	1.65 (1.13–2.40)	0.012
Tobacco smoking					
No	179 (95.2)	680 (95.8)	859 (95.7)	1.00	
Yes	9 (4.8)	30 (4.2)	39 (4.3)	1.14 (0.53–2.44)	0.893
Knowledge of HIV/AIDS					
Good (≥5)	164 (87.2)	622 (87.6)	786 (87.5)	1.00	
Poor (≤4)	24 (12.8)	88 (12.4)	112 (12.5)	1.03 (0.63–1.67)	0.990
Regimen					
1st line	184 (97.9)	695 (97.9)	879 (97.9)	1.00	
2nd line	4 (2.1)	15 (2.1)	19 (2.1)	1.00 (0.33–3.07)	1.000
Regimen drugs					
3TC+TDF+EFV or NVP	10 (5.3)	67 (9.4)	77 (8.6)	1.00	
3TC+AZT+EFV or NVP or LPV/rit	165 (87.8)	575 (81.0)	740 (82.4)	1.92 (0.96–3.82)	0.080
3TC+D4T+EFV or NVP	9 (4.8)	53 (7.5)	62 (6.9)	1.13 (0.43–3.00)	0.990
ABC+DDI+LPV/r	4 (2.1)	15 (2.1)	19 (2.1)	1.78 (0.49–6.47)	0.597
Pill burden					
1–4	169 (89.9)	650 (91.5)	819 (91.2)	1.00	
≥5	19 (10.1)	60 (8.5)	79 (8.8)	1.21 (0.70–2.09)	0.570
Frequency of ART					
Once/day	5 (2.7)	45 (6.3)	50 (5.6)	1.00	
Twice/day	179 (95.2)	650 (91.5)	829 (92.3)	2.47 (0.96–6.33)	0.075