

Adherence and Risk Behaviour in Patients with HIV Infection Receiving Antiretroviral Therapy in Bangkok

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Abstract: It could be postulated that due to lifestyle factors, patients with poor antiretroviral therapy (ART) adherence may also have risky sexual behaviour potentially leading to HIV transmission. There are limited data regarding unprotected sex risk and ART adherence in resource limited settings and our study set out to investigate these in an HIV clinic in Bangkok. Patients completed an anonymous questionnaire regarding their relationship details, ART adherence, sexual behaviour, alcohol and drug use and HIV transmission beliefs. Laboratory findings and medical history were also collected. Unprotected sex risk (USR) was defined as inconsistent condom use with a partner of negative or unknown HIV status. Five hundred and twelve patients completed the questionnaire. Fifty seven per cent of patients reported having taken ARV >95% of the time in the last month and 58% had been sexually active in the previous 30 days. Only 27 patients (5%) were classified as having USR in our cohort. Multivariate analysis showed USR was associated with female gender (OR 2.9, 95% CI 1.2-7.0, $p=0.02$) but not with adherence, age, type or number of partners, recreational drug or alcohol use nor beliefs about HIV transmission whilst taking ART. Levels of USR in this resource limited setting were reassuringly low and not associated with poor ART adherence; as all USR patients had undetectable viral loads onward HIV transmission risk is likely to be low but not negligible. Nonetheless condom negotiation techniques, particularly in women, may be useful in this group.

Keywords: Adherence, Antiretroviral therapy (ART), HIV-1 infection, Unprotected sex risk, Thailand.

INTRODUCTION

It is well established that adherence to effective antiretroviral treatment (ART) is essential for viral control and hence survival in HIV/AIDS [1]. Earlier studies have shown that ART requires strict dosing schedules for it to be maximally effective, i.e. adherence of >95% is needed for optimal viral suppression in patients taking protease inhibitor-based regimens [2]. More recent studies suggest that adherence of 80% (or even less in some patients) may be sufficient for suppression in the current era of more effective ART, particularly with a longer duration on ART[3, 4].

Having a low serum viral load (VL) is known to be associated with much lower risks of transmission of HIV [5, 6]. However it has been shown that a low plasma viral load does not always correlate with a low genital HIV viral load so transmission could still potentially occur in this situation [7-9]. Yet several studies have shown none or few heterosexual transmissions when a partner is on ART, including a recent randomised controlled international study,

HPTN052 showing a 96% transmission in discordant couples if the infected person takes ART [10, 11].

There has been conflicting information regarding the impact of ART use and sexual behaviour: some studies (particularly in resource rich countries) showing increased risk behaviour [12] while others showing a reduction in risk behaviour with ART [13-16]. One study suggested that since ART availability there may be some evidence of increased risky behaviour in non-HIV infected people [17]. Several studies have shown that the belief that having an undetectable viral load leads to lower infectiousness is associated with greater number of partners & less condom use[18-21].

Many studies have shown a link between risky sexual behaviour and alcohol and substance abuse use in HIV positive and HIV negative people[22-25]. Some studies have suggested there is a link between poor adherence to ART and increased rates of unprotected sexual intercourse [26, 27], but data from resource limited settings is limited. Poor adherence could be related to erratic lifestyle and health choices; condom use can also be affected by these factors so one could predict the other. Patients with worse adherence are more likely to have detectable VLs, if they then have unsafe sex they could potentially transmit drug-resistant HIV [28]. A study in USA showed an association between poor

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adherence, perceived HIV viral load and increased number of sexual partners [18].

Few studies regarding adherence in Thailand have been reported; one showed good levels [29] but did not assess any correlation with unprotected sex risk. Our study aimed to assess the association in the levels of adherence in chronically infected Thai HIV positive people on stable ART and risky sexual behaviour which could lead to HIV transmission. It also explored use of alcohol, recreational drugs and patients' beliefs regarding HIV transmission and whether these were related to having unprotected sex.

METHODS

This cross sectional study had ethical approval in both Thailand and Australia. All patients attending a research clinic in Bangkok, who were either on an active clinical trial or on lifelong follow-up post clinical trial and taking ART for at least 6 months between August 2007 and November 2007, were invited to join the study. Participants were asked to fill out an anonymous, self administered questionnaire in Thai regarding their relationship details, ART adherence, sexual behaviour, alcohol and drug use[30]. Adherence in the previous 30 days was assessed using a visual analogue scale (VAS) where patients indicated on a graduated line how often in the past month they took their ART from 0% (never took it) to 100% (did not miss a dose). Risk behaviours were assessed using questions adapted from validated questionnaires previously used in Thailand [31-33]. This included questions regarding sexual activity in the last 30 days in terms of frequency, numbers/type of partners and condom use. Beliefs regarding HIV transmission were ascertained. A study team member accessed patient notes and computer results system for additional information about medical history and VL/CD4 results closest to date of questionnaire completion. Patients were defined as having unprotected sex risk (USR) if they had any unprotected sex with partners of negative or unknown HIV status in the last 30 days. Patients had no financial compensation for partaking in the study. This study is registered at www.clinicaltrial.gov number NCT00511056.

Statistical Analysis

Questionnaire responses were entered into a database and patient characteristics were summarised and frequency tables of questionnaire responses were constructed. Whether a patient met our definition of unprotected sex risk (USR) or not was used as the outcome variable in logistic regression models. Covariates assessed for their predictive value were age, gender, education, income, years since HIV diagnosis, years on ART, adherence (dichotomised as good, VAS>95%, or bad, VAS ≤95% adherence), type of partner, Viral load results, alcohol & drug use, belief about HIV transmission in relation to VL or ART. Covariates significant at the level of 0.1 were used to construct a multivariate model. Statistical analysis was conducted using STATA 11.2 (Statacorp, College Station, Tx, USA)

RESULTS

Demographics

Five hundred and twelve patients completed the questionnaire and characteristics are summarised in Table 1. The median age was 39 years, 286 (56%) were male. Four

hundred and thirty five (85%) patients identified themselves heterosexual, 61 (12%) men who had sex with men (MSM) and 15 (3%) bisexual. The median current CD4 cell count was 511 (IQR 378 – 669) cells/mm³; 489 (96%) had a VL<50copies/mL. Median length of time since HIV diagnosis was 7 (IQR 4 – 9) years and median duration on ART was 5 (IQR 3 – 7) years. Most patients (71%) were earning <10,000 THB per month (approx 330 USD).

Table 1. Demographics & HIV Characteristics (n=512)

Gender	n,%
Male	286 (56)
female	226 (44)
Age in years	
Median (IQR)	39 (35 – 45), range 24 - 66
Sexuality	n,%
Heterosexual	435 (85)
MSM	61 (12)
Bisexual	15 (3)
Refused to answer	1
Education –highest level attained	n,%
Primary school	134 (26)
High school	143 (28)
College	110 (21)
Bachelor degree	116 (23)
Masters/doctorate	7 (1.5)
No answer	2 (0.5)
Income (Thai baht/month)	n,%
<5,000	171 (33)
5,001-10,000	198 (39)
10,001-20,000	103 (20)
>20,000	31(6)
No answer	9 (2)
Current CD4 (cells/mm ³)	
Median (IQR)	511 (378-669)
Viral load, copies/mL	n,%
<50	489 (96)
>50 & <200	9 (2)
>200	14 (2)
Years since HIV diagnosis	
Median (IQR)	7 (4 – 9)
Years of ART	
Median (IQR)	5 (3 – 7)

Numbers may vary due to missing data.

Partner Information

Three hundred and forty (66%) reported having partners: 178 (35%) had a partner who was also HIV positive, 109 (21%) HIV negative partners and 53 (10%) partners were of unknown HIV status. Two hundred and seventy five (80%) had disclosed their HIV status to partners.

ART Adherence

According to self-reported adherence by VAS, 288 (57%) patients took ≥95%, 178 (35%) took between 80 to

<95% and 42/508 (8%) took <80% of prescribed doses in the previous month. Eleven out of 14 patients with a VL >200copies/mL had a VAS<95%. The odds ratio for having a detectable VL >200 copies/mL with an adherence cut point of <95% on VAS was 5.0 (95%CI 1.4 – 18.2); $p = 0.01$. In the 236 patients who had recently missed dose(s) or taken doses more than 1hour late, the commonest reasons given were forgetting to take the medicines with them (51%) and travelling away from home (40%).

Sexual Behaviour

In the previous 30 days, 298 (58%) patients had engaged in sex. For 224 (75%) this was with a regular partner/s and 68 (23%) with a non primary partner (8 did not respond).

Most patients (255, 86%) had had sex with only one partner in the last 30 days, 22 (7%) with 2 partners and 6 patients with 3 or more partners (including one patient with 10 partners). Condoms were consistently used by 240 respondents (81%). Reasons given for not using a condom were most commonly due to lack of availability/preparation (28%) and the respondent or partner not liking using condoms (34%). See Table 2.

Table 2. Condom Use and Reasons for Non Use in Last 30 Days in the 298 Sexually Active Patients

Condom use (n,%)	
Always	240(81)
Almost always	16(5)
Sometimes	22(7)
Never	18(6)
No answer given	2(1)
Reasons for not using a condom in last 30 days*, n(%)	
Condoms do not feel natural/partner does not like	26(34)
Condoms were not available/I did not prepare for using a condom	21(28)
Partner also HIV positive so do not use	14(18)
Trying to conceive	5(7)
Believing that being on HAART will not spread/acquire HIV	4(5)
Fear of partner knowing HIV status	4(5)
Being drunk	2(3)

*Patients could give more than one reason.

Alcohol and Drug Use

When asked about alcohol intake in the last 30 days, 326 (64%) had had none, 140 (27%) had alcohol once or less a week, 32 (6%) 2-3 times per week and 9 (2%) had it 4 or more times per week. Sixty-eight patients had alcohol before/during sex in the last 30 days and of these 15 (22%) did not subsequently consistently use a condom. Nine had HIV-positive partners, 5 had HIV-negative/unknown status partners (1 refused to answer).

Recreational drugs were used by 10 (2%) patients, \leq once a week in all. Three used marijuana, 2 benzodiazepines, 1 poppers and the others did not specify what drug(s) was used. Four of ten (40%) used these drugs before or during sex and 2 patients did not always subsequently use condoms. Both of these had VL < 50 copies/mL and one had a partner of unknown HIV status.

Patients with Unprotected Sex Risk (USR)

Twenty seven patients (5%) fitted the criteria of having a USR, i.e., having any unprotected sex with a partner of negative or unknown HIV status in the last 30 days: 18(67%) were women; 9 were men (6 heterosexual, 2 MSM, 1 bisexual). All had undetectable viral loads and had been on HAART for at least 2 years. VAS results showed 46% reported adherence $\geq 95\%$; this was not significantly different to the non-USR population ($p=0.2$). Twenty (77%) were having sex with their primary partners and 6 with non-primary/casual partners (1 no answer). The commonest reason given for not using a condom was that their partner did not like using condoms (11, 41%); 9(33%) said that no condoms were available/they didn't prepare for condom and 2 women did not use a condom for fear of partner discovering status. No USR patients were trying to conceive or believed that being on ART meant they would not spread HIV or were drunk when they had unprotected sex. Seventeen (63%) patients with USR had disclosed their HIV status to their primary partner. In univariate analysis USR was not associated with poor ART adherence (VAS either <80 or 95%), alcohol/drug use, casual partners, time on ART or the belief that being on ART prevented transmitting HIV (see Table 3). Younger age (<40years), low education, lower income and female gender were all associated with USR, but after adjustment in a multivariate model, only female gender was significant (odds ratio 2.9; 95% confidence interval [CI] 1.2 -7.0; $P = 0.02$).

Patients' Beliefs Regarding HIV Transmission and HAART

When asked if taking HIV medicine reduces the threat of transmitting HIV to others 132 (26%) agreed, 286 (56%) did not and 90 (18%) were unsure. When asked if they thought that having an undetectable viral load (<50 copies) reduces the threat of transmitting HIV to others 99 (19%) agreed, 294 (57%) disagreed and 114 (22%) were unsure. When asked if taking HIV medicine reduces their concerns about having sex without using a condom 31 (6%) said yes, 424 (83%) said no and 49 (10%) were unsure.

DISCUSSION

The adherence rates in our cohort were lower than expected with only 57% reporting adherence of $\geq 95\%$ in the last 30 days on the visual analogue scale, but despite this the viral loads in our cohort were suppressed in the majority (96%) of patients. This finding agrees with other studies noting that the current more potent ART may be more forgiving than previously thought[3]. Unsurprisingly patients reporting a VAS <95% had a higher rates of viral loads >200copies/mL (OR 5.0). A small number of the patients with very low reported adherence (i.e. 5-45% on VAS) had undetectable viral loads so miscomprehension of the VAS instructions is a possible explanation although it has previously been well understood in a similar patient group[34]. Conversely some patients with excellent reported adherence had detectable VLs but may have been on failing regimes and waiting for regimen change or resistance results. Pill counts were not done to confirm reported adherence. Reasons for forgetting ART were in the majority practical issues of forgetting to bring the medications with them and

Table 3. Predictive Factors for Unprotected Sex Risk (USR) in the Previous 30 Days

Risk Factor	Univariate		Multivariate	
	OR (95% CI)	P	OR (95% CI)	P
Female gender	4.2 (1.8 – 9.8)	0.001	2.9 (1.2 -7.0)	0.02
Primary school education or less	2.6 (1.1 – 5.9)	0.02	1.9 (0.7 – 4.7)	0.19
Age <40years	3.2 (1.2 - 8.6)	0.03	2.3 (0.79 – 6.5)	0.13
Low income<5,000THB/month	2.7 (1.2 – 6.1)	0.02	1.6 (0.65 – 4.1)	0.29
More than 1 partner in last 30 days	1.03 (0.34 – 3.15)	0.95		
Any alcohol in last 30 days	1.1 (0.51 – 2.47)	0.78		
Recreational drug use in last 30 days	3.1 (0.62 – 16.0)	0.17		
Taking HAART for ≤ 2 years	0.97 (0.39 – 2.38)	0.94		
< 95% adherence on VAS	1.6 (0.7 – 3.5)	0.27		
< 80% adherence on VAS	1.4 (0.4 – 5.0)	0.61		
Sex with primary (vs non-primary) partner	0.80 (0.32 – 1.90)	0.61		
Believing transmission is reduced if on HAART & viral load <50 copies/mL	0.98 (0.35 – 2.71)	0.97		

travelling away from home. This could be potentially be remedied by providing easier more discreet packaging i.e. small pill boxes that can be kept in a pocket/bag at all times.

More than half (58%) of the patients were sexually active in the last 30 days and in the majority (80%) a condom was always used; this rate of condom use is higher than found in cohorts in Kenya (72%) and Uganda (66%) [35, 36]. In those 56(19%) who did not always use a condom, more than half had a known HIV positive partner. The risk of an HIV positive person potentially passing on or acquiring another HIV virus appears to be minimal and the larger concern in this small group of seroconcordant couples would be acquiring sexually transmitted diseases and for females of becoming pregnant[37, 38]. Indeed, trying to conceive was a reason for non condom use in nearly 7%. Information on type of sex was not collected but each type is known to have different risks [39, 40]. Interestingly nearly 28% of patients reported the lack of availability and/or lack of planning as a reason for non condom use. Condoms are given out for free to all patients in the HIV clinic so it is more likely that the lack of planning for sexual activity was the cause and patients need to be encouraged to carry condoms on them to be prepared.

Only 27 out of 512 (5%) were classified as USR (having had any unprotected sexual intercourse with a partner of negative or unknown HIV status in the last 30days). This is reassuringly low. The adherence in this group of patients was lower (46 vs 57%) than non-USR patients but this was not statistically significant and indeed despite this all USR patients had VL <50copies/mL. No information on sexually transmitted diseases was available but a previous study of 824 HIV positive asymptomatic patients in Bangkok showed *Chlamydia trachomatis* rates of 9.7% and *Neisseria gonorrhoeae* of 1.3%, with a high disease burden in sex workers and in younger patients; it is likely our cohort would have lower rates than this with an older median age (39years) and no sex workers [41]. Genital HIV RNA levels were not collected and the true potential infectivity of this

small but important group of patients in this cohort is unknown but likely to be very small. Contrary to expectations there was no association of USR and poor adherence in this group. This association may not have been found due to small patient numbers exhibiting USR but may indicate that the unprotected sex was not due to 'erratic' lifestyles but rather due to other sex-related factors such as condom issues and HIV disclosure concerns. Indeed 40% reported their partner's dislike of condoms as the reason for unprotected sexual intercourse. This exemplifies the complex nature of sexual risks including the importance of condom negotiation skills, particularly for women (who made up 67% of USR). Female gender was the only factor associated with increased risk of USR (OR 2.9). Ragnarsson *et al.*, recently reported a similar finding in a cohort in Kenya with female gender having an OR of 3.03 for inconsistent condom use [35]. This group suggested possible reasons for their finding being a lack of individual negotiating power in intimate relationships and also reproductive desires; in our study none of the USR women reported reproductive desire as their reason for non condom use so difficulty with condom negotiation or partner choice are likely factors in our cohort and further work needs to be done e.g. acceptability testing of other barrier methods such as the female condom and teaching condom negotiation techniques.

In the questions regarding beliefs only 26% patients thought that taking ART would reduce transmission of HIV yet even fewer patients believed that having an undetectable viral load would affect HIV transmission. This study was carried out when there was less evidence regarding ART and HIV transmission, also many of the patients in the cohort have low incomes and may not have access to the latest HIV news e.g. through the internet and networks, to guide their decision making in unprotected sex risk. Medical staff discussing latest scientific information regarding transmission with patients need to clearly state the evidence so far and carefully tailor their advice to a patient's

individual situation to ensure partners are not inadvertently put at risk.

Only a small proportion of patients reported recreational drug use and over 2/3 did not drink alcohol; this implies that this cohort is not a high 'risk taking' group, either because of self selection by being someone willing to enter into a clinical trial or due to the regular counselling and advice given regarding risk behaviours, or likely a combination of both these factors. Of those who drank alcohol around the time of sex 22% did not subsequently use a condom and this supports findings of many other studies showing alcohol intake can lead to subsequent unsafe sexual practises[23, 24].

Limitations of this study include the fact that this was performed in a research setting so results may not be transferable to the general population where less intense medical input and counselling related to sexual risk and adherence may occur. Patients were only asked about sexual activity in the last 30 days which may have underestimated true sexual activity and hence risk behaviour in the cohort. The number of MSM in the cohort was low reflecting the epidemic of HIV in Thailand being largely heterosexual.

In summary unprotected sex risk was uncommon (27/512, 5%) and poor ART adherence was not associated with USR in this resource limited cohort. Women were significantly more likely to have USR and more work needs to be done to help women in condom negotiation particularly in serodiscordant relationships. HIV prevention strategies need to be focused on high transmission risk groups to be maximally effective (i.e. patients not on ART, seroconverting patients, undiagnosed patients) and this outpatient clinic cohort appears to have a reassuring low, although not negligible, risk of transmission.

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CONFLICTS OF INTEREST

Declared none.

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