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TAHOD
HIV Observational Database

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Impact of sex on long-term treatment outcomes of highly active antiretroviral therapy (HAART) in the TREAT Asia HIV Observational Database

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Introduction

Numerous studies have evaluated potential differences between men and women in the course of HIV infection, response to treatment, and drug pharmacokinetics. [1-3] However, most of these studies had short-term follow up (6 to 12 months). Besides, clinical data on the impact of sex are lacking for HIV-infected patients from the Asia-Pacific. Better understanding of the differences between men and women in this region may enhance individualization of treatment and improve efficacy and safety outcomes of HAART. The study objective was to evaluate the effect of sex on viro-immunological responses to HAART, treatment outcomes and toxicities in the Asia-Pacific.

Methods

The TREAT Asia HIV Observational Database (TAHOD) is a collaborative observational cohort study involving 18 sites in the Asia-Pacific region (See acknowledgements). Detailed methods are published elsewhere. [4] Briefly, each site recruited approximately 200-300 HIV-infected patients, including both patients on or not yet initiating antiretroviral therapy. Recruitment was based on a consecutive series of patients regularly attending a given site from a particular start-up time.

TAHOD has been collecting prospective clinical data of HIV-infected patients in the Asia-Pacific since 2003. The following data were collected: patient demographics and baseline data, CD4 and CD8 count, HIV viral load level, prior and new AIDS defining illness (ADI), date and cause of death, prior and current prescribed HAART, and reason for treatment change. Endpoints of this study included change in CD4 counts and proportion with undetectable HIV viral load at 96 weeks after HAART initiation; rate of new AIDS or death, loss to follow-up (defined as not seen in clinic for more than 12 months), and treatment change due to toxicity. Frequency of CD4 and HIV viral load monitoring during the study period was also measured. Results were compared between males and females.

Forward stepwise multivariate linear regression and logistic regression models were used to evaluate the independent associations of different baseline variables with change in CD4 counts and proportion of patients reaching undetectable HIV viral load (<500 copies/mL) at 96 weeks. Multivariate Cox proportional hazards models were used to determine predictors of new AIDS or death, loss to follow-up, and treatment change due to toxicity. P <0.05 for a two-sided test was considered to be statistically significant.

Results

A total of 3,899 patients (71% male and 29% female) were evaluated. Table 1 shows the baseline characteristics of the patients at HAART initiation. Significant differences were found between males and females in the following baseline parameters: median age (35 years vs. 34 years, p <0.001), reported injecting drug use (8% vs. 2%, p <0.001), CDC category C (45% vs. 34%, p <0.001), HIV viral load (median 4.9 log vs. 4.8, p=0.03), HBV (12% vs. 6%, p <0.001), HCV (15% vs. 9%, p <0.001), and presence of anemia (52% vs. 44%, p <0.001).

Table 1: Baseline characteristics by sex at HAART initiation

	Total (n=3899)	Male (n=2761)	Female (n=1138)	p value
Median age [years(IQR)]	35 (30-41)	35 (30-42)	34 (29-40)	<0.001
Mode of infection				
Heterosexual contact	2648 (68%)	1645 (60%)	1003 (88%)	
Homosexual contact	685 (17%)	676 (24%)	9 (1%)	
Injecting drug use	233 (6%)	212 (8%)	21 (2%)	
Blood products	66 (2%)	46 (2%)	20 (2%)	
Others	267 (7%)	182 (6%)	85 (7%)	<0.001
CDC clinical classification				
Category A	1877 (48%)	1288 (47%)	589 (52%)	
Category B	396 (10%)	235 (8%)	161 (14%)	
Category C	1626 (42%)	1238 (45%)	388 (34%)	<0.001
Median CD4 cell count [cells/μL(IQR)]	113 (39-206)	108 (35-206)	128 (44-203)	0.094
Median HIV viral load [log copies/mL(IQR)]	4.9 (4.1-5.5)	4.9 (4.2-5.5)	4.8 (3.9-5.4)	0.029
Hepatitis B coinfection	269 (10%)	220 (12%)	49 (6%)	<0.001
Hepatitis C coinfection	291 (13%)	236 (15%)	55 (9%)	<0.001
Presence of anemia	1166 (50%)	861 (52%)	305 (44%)	<0.001
Prior treatment (mono or dual) before cART	511 (13%)	377 (14%)	134 (12%)	0.114

Anemia - male <13g/dL and female <11 g/dL; cART - combination antiretroviral therapy

There was no significant difference by sex in CD4 change at 96 weeks (225 vs. 223 cells/μL, p=0.60). However, females were more likely to reach undetectable HIV viral load at 96 weeks after adjustment for other variables (OR 1.7, p=0.024). Table 2 summarizes the factors associated with undetectable HIV viral load.

Table 2: Factors associated with undetectable HIV viral load at 96 weeks after adjustment for other variables

	Multivariate	
Variable	**OR (95% CI)**	**p value**
Sex		
Male*	1	
Female	1.7 (1.1-2.6)	0.024
Age group, years		
≦25*	1	
26-25	2.0 (1.2-3.5)	0.011
36-45	2.4 (1.4-4.3)	0.002
≧46	3.1 (1.6-6.1)	0.001
Mode of infection		
Heterosexual*	1	
Homosexual	1.3 (0.9-2.1)	0.165
IDU	0.2 (0.1-0.5)	<0.001
Blood product	1.1 (0.2-5.0)	0.926
Other/unknown	1.6 (0.7-3.6)	0.283
Prior mono/dual ART		
No*	1	
Yes	0.4 (0.3-0.6)	<0.001

* Baseline category. IDU - injecting drug use; ART - antiretroviral therapy

Sex was not a predictor of new AIDS or death (adjusted HR 0.83, 95% CI 0.62 – 1.10) or loss to follow-up (adjusted HR 1.04, 95% CI 0.8 – 1.2). In contrast, females were more likely to change treatment regimen due to toxicity (adjusted HR 1.9, 95% CI 1.4 – 2.7). Figure 1 illustrates the time to AIDS or death, and Figure 2 reports treatment change due to toxicity. Frequency of HIV viral load monitoring differed by sex (median days between tests: 180 days in males vs. 238 days in females, p <0.001).

Figure 1: Time to new AIDS or death, by sex

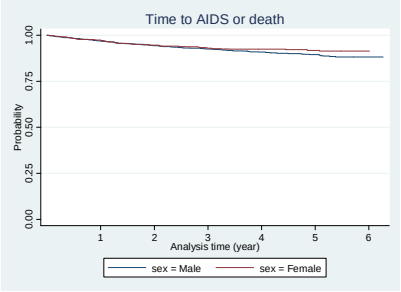
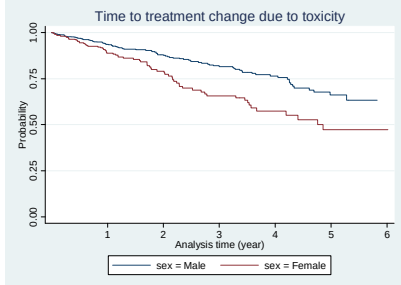


Figure 2: Time to treatment change due to toxicity, by sex



Conclusion

There was no significant difference in the risk of developing new AIDS and death between male and female patients from TAHOD. Multivariate analysis showed that a higher proportion of females achieved undetectable HIV viral load at 96 weeks despite the fact that they were more likely to change treatment regimen due to toxicity. However, women had less frequent viral load testing, which may be a surrogate marker for reduced access to and/or uptake of care. Further study is warranted to address possible inequalities in care delivery.

References:

1. Kuyper LM, Wood E, Montaner JS et al. Gender differences in HIV-1 RNA rebound attributed to incomplete antiretroviral adherence among HIV-1 infected patients in a population-based cohort. J Acquir Immune Defic Syndr 2004; 37: 1470-6.
2. Collazos J, Asensi V, Carton JA et al. Sex differences in the clinical, immunological and virological parameters of HIV-infected patients with HAART. AIDS 2007; 21: 835-43.
3. Nicastri E, Leone S, Angeletti C et al. Sex issues in HIV-1 infected persons during highly active antiretroviral therapy: a systematic review. J Acquir Immune Defic Syndr 2007; 60: 724-32.
4. Zhou J, Kumarasamy N, Ditangco R et al. The TREAT Asia HIV Observational Database: baseline and retrospective data. J Acquir Immune Defic Syndr 2005; 38: 174-9.

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