The TREAT Asia HIV Observational Database: baseline and retrospective data

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Introduction

Relatively little is known regarding HIV disease natural history and response to antiretroviral treatments among Asian people infected with HIV. The Therapeutics Research, Education and AIDS Training (TREAT) Asia is a cooperative network of clinicians throughout Asia and the Pacific that aims to expand capacity for the broader introduction of HIV/AIDS treatments in the region. The TREAT Asia HIV Observational Database (TAHOD) is the first collaborative study by the TREAT Asia network. TAHOD is a multi-centre, observational study of patients with HIV and aims to assess HIV disease natural history in treated and untreated patients in the Asia and Pacific region.

The objectives of this study are first, to describe TAHOD working procedure and methods; second, to summarise baseline data on patients so far recruited to TAHOD and third, to assess baseline and retrospective data, the rate of CD4 decline in untreated patients and the CD4 and viral load response in patients receiving antiretroviral treatment.

Methods

TAHOD is a collaborative observational cohort study of 11 sites in the Asia and Pacific region (appendix) and aims to recruit and follow-up 200 patients from each site, including both treated and untreated patients. To ensure maximal follow-up rates, recruitment is based on a consecutive series of patients regularly attending a given site.

Ethical approval for the study was obtained from the University of New South Wales Ethics Committee. Each site also approached a local ethics committee for approval. Since all data forwarded to the NCHECR are in an anonymous fashion, informed consent of subjects was not a requirement of sites, except if a requirement of a site's local ethics committee.

Patient demography, stage of disease and antiretroviral treatment data are collected. Retrospective data are collected where available. All data are entirely observational, with test or intervention performed only to clinical guideline at each site. Data are transferred electronically in password-protected WINZIP format to the National Centre in HIV Epidemiology and Clinical Research (NCHECR) for central aggregation and analysis in March and September each year. We present here summaries of the initial baseline data transferred up to November 2003.

Results

By the end of November 2003, 1283 patients had been recruited to TAHOD (**Table 1**). The majority of the patients were male, with median age 36 years. Chinese, Indian and Thai were the main ethnic groups. Most patients were infected through heterosexual contact; around 8% through homosexual contact and very few (less than 1%) through injecting drug use only.

39% of patients had a previous AIDS defining illnesses (**Table 2**), of which, 54% had tuberculosis, and 23% Pneumocystis carinii pneumonia. 9% of all the patients had a CDC category B illness and 5% had Papular pruritic eruption but without AIDS. Most of the patients had a baseline CD4 count between 200-499 cells/µl (48%)and a HIV viral load below 400 copies/ml (62%).

230 patients had more than one CD4 count reported retrospectively while not on antiretroviral treatment. The average rate of CD4 change (per month since the first CD4 count) was –2.8 cells/µl (95% confidence interval, CI –6.4 to 0.7, p=0.1, **Table 3**). Independent factors associated with a higher rate of decreasing CD4 were found to be patients who acquired HIV through heterosexual contact (compared to other route of transmission) and a higher baseline CD4 count (compared to a lower CD4 count at baseline).

Retrospective data were available for 308 patients who had at least one CD4 count before starting highly active antiretroviral therapy (HAART) and another CD4 count six month (within 3 to 9 month) after starting HAART. The mean change was 109.3 cells/µl (95% CI 95.3-123.3, p<0.001, **Table 4**). Independent factors associated with a smaller rate of increasing CD4 included female gender, a higher level of CD4 count before starting HAART and prior treatment with mono or double therapy.

120 patients had at least one HIV viral load test before starting HAART and another viral load test six months (within 3 to 9 month) after starting HAART. 63% of patients had a viral load below the detectable level (<400 copies/ml, **Table 5**). Older age was the only factor associated with a significantly higher rate of achieving undetectable viral load after starting HAART.

Table 1: Patient characteristics.

N⁰ patients by site*:	CN-BJ	70	(5%)	
	CN-HK	55	(4%)	
	TW-TP	94	(7%)	
	IN-YRG	202	(16%)	
	IN-PUNE	123	(10%)	
	MY-GH	82	(6%)	
	MY-UH	200	(16%)	
	PH-RITM	70	(5%)	
	SG-TTSH	87	(7%)	
	TH-CHULA	200	(16%)	
	TH-RAMA	100	(8%)	
	Total	***1283***		
Age (years)**	median (range)	36	(19-90)	(77 missing)
	<20	3	(<1%)	
	20-29	200	(16%)	
	30-39	596	(46%)	
	40-49	278	(22%)	
	50+	131	(10%)	
Gender	Male	940	(73%)	
	Female	342	(27%)	
	Transgender	1	(<1%)	
Ethnicity	Caucasian	5	(<1%)	(16 missing)
	Chines	500	(39%)	
	Indian	343	(27%)	
	Malay	25	(2%)	
	Philippine	72	(6%)	
	Thai	314	(24%)	
	Other	8	(<1%)	
Exposure category	Homosexual contact	107	(8%)	(81 missing)
	Homosexual & IDU	1	(<1%)	
	IDU only	6	(<1%)	
	Heterosexual contact	964	(75%)	
	Heterosexual & IDU	16	(1%)	
	Receipt of blood/products	20	(2%)	
	Other	88	(7%)	
First year diagnosed with HIV	1996	95	(9%)	(184 missing)
	1996-2000	425	(39%)	
	2001-2002	393	(36%)	
	2003	186	(17%)	
CDC classification for HIV infection***	Category A	661	(52%)	
	Category B	118	(9%)	
	Category C	504	(39%)	
Baseline CD4 count (cells/µ?l)**	<50	90	(10%)	
	50-199	258	(28%)	
	200-499	435	(47%)	
	500+	137	(15%)	
	Median (range)	263	(2-1220)	
	Not tested	361		
HIV viral load (copies/m?l)**	Not detectable (<400)	390	(63%)	
	400-10000	78	(12%)	
	10000+	157	(25%)	
	Median (range)	1400	(<400 – >750000)	
	Not tested	656		
Current antiretroviral treatment (from Jan 2003 to present, among 1121 patients)	None	465	(41%)	
	Mono/dual therapy	42	(4%)	
	3+,NRTI+/-PI,no NNRTI	100	(9%)	
	3+,NRTI+NNRTI,no PI	488	(44%)	
	3+,NNRTI+PI	26	(2%)	

* Site code:
CN-BJ, Ditan Hospital, Beijing, China;
CN-HK, Queen Elizabeth Hospital, Hong Kong, China;
TW-TP, Taipei Veterans General Hospital and AIDS Prevention and Research Centre, National Yang-Ming University, Taipei, Taiwan
IN-YRG, YRG Centre for AIDS Research and Education, Chennai, India;
IN-PUNE, HIV Project, Ruby Hall Clinic, Pune, India;
MY-GH, Hospital Kuala Lumpur, Kuala Lumpur, Malaysia;
MY-UH, University of Malaya, Kuala Lumpur, Malaysia;
PH-RITM, Research Institute for Tropical Medicine, Manila, Philippine;
SG-TTSH, Tan Tock Seng Hospital, Singapore;
TH-CHULA, HIV-NAT/The Thai Red Cross AIDS Research Centre, Bangkok, Thailand;
TH-RAMA, Ramathibodi Hospital, Bangkok, Thailand.

** Age, CD4 count, HIV viral load at time of entry into TAHOD (CD4 within 180 days, viral load within 365 days).

*** Centre for Disease Control. 1993 Revised Classification System for HIV Infection and Expanded Surveillance Case Definition for AIDS Among Adolescents and Adults, Morbidity and Mortality Weekly Reports 41(RR-17), December 18 1992.

Table 2: Type of prior AIDS among patients with AIDS and among all TAHOD patients*.

AIDS	N⁰ patients	% patient with AIDS	% all patients
TB	273	54.38	21.28
PCP	115	22.91	8.96
Penicilliosis	43	8.57	3.35
Salmonella septicaemia	36	7.17	2.81
Oesophageal candidiasis	32	6.37	2.49
Herpes simplex	29	5.78	2.26
Cryptococcosis/extrapulmonary	28	5.58	2.18
Cytomegalovirus retinitis	26	5.18	2.03
Toxoplasmosis	19	3.78	1.48
Non-TB mycobacterial diseases	14	2.79	1.09
Candidiasis/bronchi, trachea, lung	12	2.39	0.94
HIV wasting syndrome	9	1.79	0.70
Cryptosporidiosis	6	1.20	0.47
Recurrent pneumonia	6	1.20	0.47
Cytomegalovirus	4	0.80	0.31
Lymphoma/brain	3	0.60	0.23
Leukoencephalopathy	3	0.60	0.23
HIV encephalopathy	2	0.40	0.16
Histoplasmosis	2	0.40	0.16
Isosporosis	2	0.40	0.16
Lymphoma/Burkitt	2	0.40	0.16
Invasive cervical cancer	1	0.20	0.08
Kaposi's sarcoma	1	0.20	0.08

* Patients can report more than one prior AIDS, but only the first AIDS of each type was count counted per patient.

Table 3: Factors associated with rate of change in CD4 counts among patients not on antiretroviral treatment.

	No. patients	Mean CD4 (cells/µl) change	Univariate difference*	Univariate p-value	Multivariate analysis difference*	Multivariate analysis p-value
Overall	**230**	**-2.8**				
Gender						
Male	166	-0.8				
Female	64	-8.1	-7.2	0.070	-3.54	0.351
Age (years)						
<31	63	-8.4				
31-40	102	-1.0	7.4	0.087	2.98	0.470
41+	53	2.3	10.7	0.034	5.92	0.214
Not known	12	-11.7	-3.3	0.701	2.19	0.783
Exposure category						
Heterosexual contact	171	-5.3				
Other	59	4.2	9.5	0.020	8.56	0.024
HBV infection						
Negative/not tested	220	-2.8				
Positive	10	-3.6	-0.8	0.926	-10.78	0.190
HCV infection						
Negative/not tested	222	-3.6				
Positive	8	17.6	21.2	0.030	17.63	0.052
CDC classification of HIV infection						
Category A	163	-2.8				
Category B	16	2.9	5.7	0.422	-1.49	0.823
Category C	51	-4.7	-1.9	0.673	-7.88	0.056
Baseline CD4 count (copies/ml)						
<200	82	11.0				
200-350	57	-14.0	-25.1	<0.001	-24.76	<0.001
351+	91	-8.3	-19.3	<0.001	-19.00	<0.001

* Differences were compared to the first category of each variable.

Table 4: Factors associated with change in CD4 counts at six month among patients receiving HAART treatment.

	No. patients	Mean CD4 (cells/µl) change	Univariate difference*	Univariate p-value	Multivariate analysis difference*	Multivariate analysis p-value
Overall	**308**	**109.3**				
Gender						
Male	239	119.3				
Female	69	74.7	-44.6	0.009	-35.05	0.030
Age (years)						
<31	54	113.3				
31-40	149	112.8	-0.5	0.980	-5.98	0.757
41+	85	95.0	-18.3	0.401	-20.20	0.326
Not known	20	132.6	19.3	0.556	3.33	0.915
Exposure category						
Heterosexual contact	218	109.6				
Other	90	108.4	-1.2	0.939	5.65	0.704
HBV infection						
Negative/not tested	298	109.6				
Positive	10	99.6	-10.0	0.803	-12.14	0.748
HCV infection						
Negative/not tested	299	109.3				
Positive	9	107.4	-1.9	0.964	-38.49	0.335
CDC classification for HIV infection						
Category A	142	92.4				
Category B	33	88.1	-4.4	0.855	-5.17	0.822
Category C	133	132.6	40.1	0.007	22.35	0.145
Baseline CD4 count (copies/µl)						
<200	224	125.1				
200-350	64	89.7	-35.4	0.039	-39.53	0.019
351+	20	-4.9	-123.0	<0.001	-120.87	<0.001
HAART**						
3+,NRTI+/-PI,no NNRTI	106	82.0				
3+,NRTI+NNRTI,no PI	197	126.2	44.2	0.003	21.10	0.164
3+,NNRTI+PI	5	22.2	-59.8	0.288	-54.46	0.310
Having mono/double therapy before starting HAART						
No	195	130.6				
Yes	113	72.5	-58.1	<0.001	-59.57	<0.001

* Differences were compared to the first category of each variable.
** HAART
3+,NRTI+/-PI,no NNRTI: combination includes NNRTI and/or PI, but excludes NNRTI.
3+,NRTI+NNRTI,no PI: combination includes at least one NNRTI, but excludes PI.
3+,NNRTI+PI: combination includes both NNRTI and PI, and/or NRTI.

Table 5: Factors associated with HIV viral load under detectable level among patients receiving HAART treatment.

	No. Patents	HIV viral load undetectable No. (%)	Univariate OR	Univariate p-value	Multivariate analysis OR (95%CI)	Multivariate analysis p-value
Overall	**120**	**75 (63%)**				
Gender						
Male	92	57 (62%)				
Female	28	18 (64%)	1.1	0.824	1.8 (0.6-5.0)	0.262
Age (years)						
<31	19	8 (42%)				
31-40	65	41 (63%)	2.3	0.108	2.3 (0.8-6.7)	0.108
41+	33	25 (76%)	4.3	0.018	5.5 (1.3-14.4)	0.018
Not known	3	1 (33%)				
Exposure category						
Heterosexual contact	78	49 (63%)				
Other	42	26 (62%)	1.0	0.921	1.0 (0.4-2.2)	0.947
HBV infection						
Negative/not tested	115	72 (63%)				
Positive	5	3 (60%)	0.9	0.906	0.8 (0.1-4.9)	0.785
HCV infection						
Negative/not tested	115	72 (63%)				
Positive	5	3 (60%)	0.9	0.906	1.0 (0.1-7.3)	0.987
CDC classification of HIV infection						
Category A	49	29 (59%)				
Category B	20	14 (70%)	1.6	0.402	1.4 (0.4-4.4)	0.571
Category C	51	32 (63%)	1.2	0.715	1.0 (0.4-2.4)	0.967
Baseline viral load test (copies/ml)						
<50000	60	42 (70%)				
50000+	60	33 (55%)	0.5	0.091	0.5 (0.2-1.1)	0.082
HAART*						
3+,NRTI+/-PI,no NNRTI	71	44 (62%)				
3+,NRTI+NNRTI,no PI	45	29 (64%)	1.1	0.788	1.1 (0.5-2.5)	0.764
3+,NNRTI+PI	4	2 (50%)	0.6	0.635	0.5 (0.06-4.5)	0.565
Having mono/double therapy before starting HAART						
No	55	30 (55%)				
Yes	65	45 (69%)	1.9	0.099	2.1 (1.0-4.6)	0.065

* HAART
3+,NRTI+/-PI,no NNRTI: combination includes NNRTI and/or PI, but excludes NNRTI.
3+,NRTI+NNRTI,no PI: combination includes at least one NNRTI, but excludes PI.
3+,NNRTI+PI: combination includes both NNRTI and PI, and/or NRTI.

Discussion

Among patients not on antiretroviral treatment, there was a non-significant decrease of CD4 count of 2.8 cells/µl per month with a higher rate of decrease found among patients infected with HIV through heterosexual contact and patients having a higher baseline CD4 count. Among patients who started HAART and had a baseline and six-month CD4 count measurement, the mean six-month CD4 count increase was 109 cells/µl. Predictors of smaller CD4 count increases were female gender, higher CD4 count before starting HAART, and prior treatment with mono or double therapy. Among patients who had started HAART and had a viral load assessment at baseline and six months, 63% of patients had undetectable viral load at six months, with older patients found to be more likely to achieve undetectable level.

Analyses of retrospective data in TAHOD suggest that the overall response to HAART in Asian patient populations is similar to that seen in developed countries. TAHOD has recruited over 1,000 patients, with over 2,000 patients expected when fully recruited. With prospective follow-up TAHOD will be able to assess the natural history of HIV disease, and response to antiretroviral treatments, in patients from the Asia and Pacific region.

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Appendix

The TREAT Asia HIV Observational Database:
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