Treatment outcomes of HIV-associated tuberculosis cases reported to the TB-HIV registry of Hong Kong from 1996 to 2008

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Introduction

HIV-associated TB carries a high fatality rate. Early initiation of HAART has been shown to improve the outcome of patients with HIV-associated TB. Nevertheless, its concurrent use with anti-TB treatment is complicated by overlapping toxicities and immune reconstitution inflammatory syndrome (IRIS). There has been a controversy on the optimal timing of HAART in patients with HIV-associated TB. The present study was undertaken to evaluate the treatment outcome of HIV-associated TB cases reported to the TB-HIV Registry of Hong Kong and address the issue of optimal timing of initiation of ART in HIV-associated TB patients.

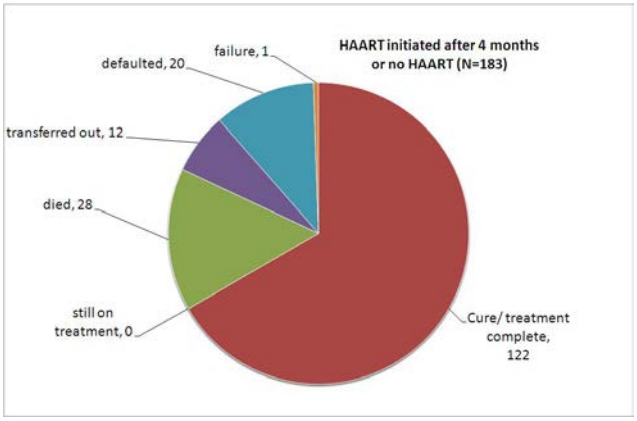
Materials and methods

The records of patients with HIV-associated TB reported to the Registry and managed at Tuberculosis and Chest Service and Special Preventive Program of Hong Kong from Jan 1996 to Dec 2008 were retrospectively reviewed. Demographic and clinical data were collected using standard data collection forms and by reviewing discharge summaries. TB treatment outcomes were defined according to recommendation from the WHO. A significant adverse effect from treatment was defined as one requiring modification of drugs. IRIS was defined as the development of recurrent, new or worsening symptoms or signs of TB or recurrent, new, or deteriorating radiological manifestations of TB that occurred after initiation of treatment. A comparison of a favourable outcome vs non-favourable outcome was made using appropriate statistical tests to identify variables that might affect treatment outcome.

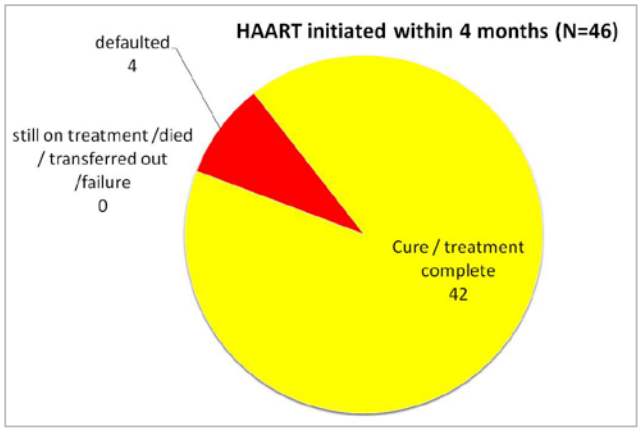
Results

Of 229 patients who were ART- naïve at TB diagnosis, 164 (71.6%) had a cure or treatment completion at 24 month. Twelve (5.2%) were transferred out and 24 (10.5%) defaulted treatment. One patient (0.4%) had treatment failure. Twenty-eight (12.2%) died during anti-TB treatment.

HAART initiated after 4 months or no HAART (N=183)



HAART initiated within 4 months (N=46)



Female sex, non-Chinese subjects, presence of bacillary drug resistance and delayed initiation of ART were found to be associated with non-favourable outcomes on univariate analysis (all $P < 0.05$) (Table 1). Delayed initiation of HAART beyond 4 month remained as the only independent predictor of non-favourable outcome from multiple logistic regression analysis ($p = 0.002$, odds ratio = 7.8, 95% CI = 2.1-28.6).

Table 1. Demographic, clinical and treatment characteristics in 229 HAART-naïve patients with HIV-associated TB and their comparison by univariate and multiple logistic regression analysis

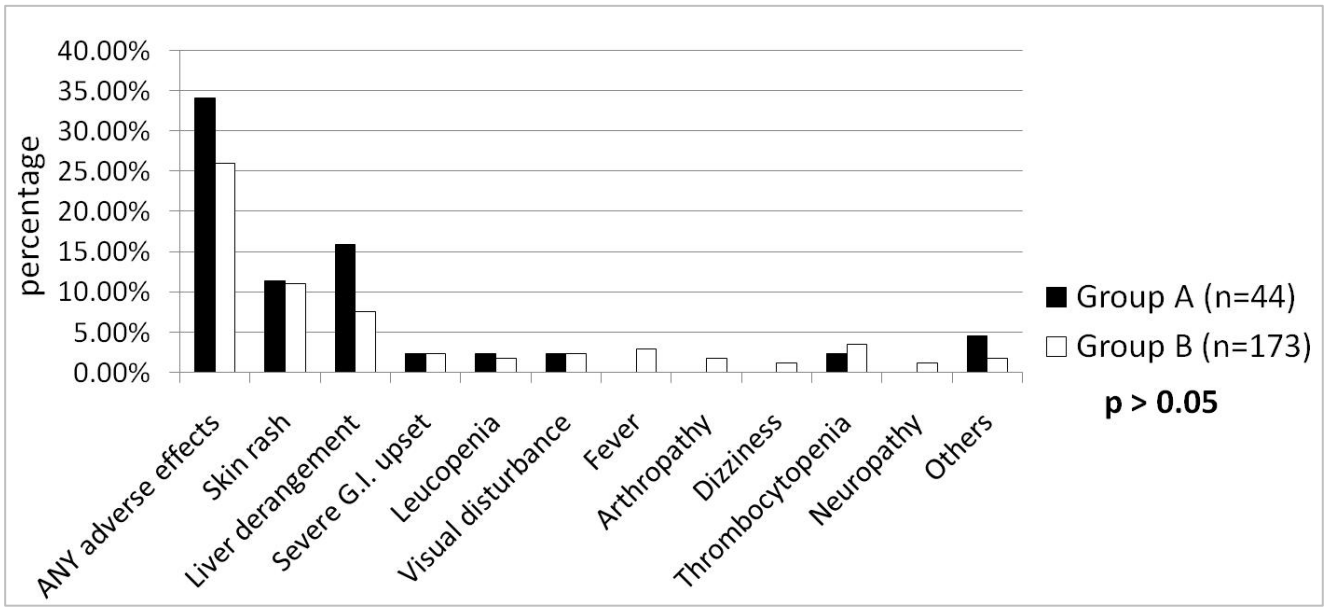
	Treatment outcomes at 24 month		Univariate analysis, P value	Multiple logistic regression analysis		
Variable	**Favourable (n = 164)**	**Non- favourable (n = 65)**		**P value**	**Odds ratio**	**95% CI**
Age	41 (20-81)	36 (19-83)	NS	NS	-	-
Female sex	14 (8.5%)	12 (18.5%)	0.038	NS	-	-
Non-Chinese	27 (16.5%)	27 (41.5%)	0.001	NS	-	-
Extra-pulmonary TB	109 (66.5%)	38 (58.5%)	NS	NS	-	-
CD_4 count* < 100 100- 199 ≧ 200	89 (58.6%) 32 (21.1%) 31 (20.4%)	31 (56.4%) 11 (20.0%) 13 (23.6%)	NS	NS	-	-
Presence of resistance to anti-TB drugs***	23 (17.3%)	9 (22.0%)	0.033	NS	-	-
ART initiated within 4 month	42 (25.6%)	4 (6.2%)	0.001	0.002	7.8	2.1-28.6

*Information on CD4 count available in 152 patients with favourable outcome and 55 patients with non-favourable outcome respectively

***Information on presence of drug sensitivity pattern available in 133 patients with favourable outcome and 41 patients with non-favourable outcome with positive cultures (any specimens) respectively

Adverse effects from anti-TB drugs tended to occur more frequently in patients with early initiation of HAART (15/44 or 34.1%) compared to the remaining patients (45/173 or 26.0%) ($P > 0.05$) (Fig. 1). A significantly higher proportion of patients with early initiation of HAART (9/46 or 19.6%) experienced immune reconstitution inflammatory syndrome than their counterpart (5/183 or 2.7%) ($P < 0.001$).

Fig.1. Significant adverse effects due to anti-TB drugs experienced by 44 patients with ART initiated within 4 months from TBDOS (Group A) and 173 patients with ART initiated after 4 months or ART not initiated during the course of anti-TB treatment (Group B)



(some patients experienced more than one significant adverse effects from TB drugs)

Although admission was frequently required for patients with IRIS, HAART could be continued in most patients and there was no death attributable to IRIS (Table 2)

Table 2. Manifestations of immune reconstitution inflammatory syndrome in 9 patients with ART initiated within 4 months from TBDOS

Patient	Sex	Age	CD_4 at IRIS	ART Regimen	Interval between IRIS and ART (m)	Clinical feature	Remark
1	M	37	52	CBV, IDV	1	Increased left lower lobe shadow and development of left pleural effusion	Hospitalization
2	M	34	98	CBV, IDV	0.5	Increased cervical lymph node, fever, night sweat	Steroid therapy, TB Px prolonged to 12 m
3	M	38	13	IDV, 3TC, AZT	1	Increased pleural effusion	Hospitalization, TB Px prolonged to 12 m
4	M	52	24	3TC, d4T, IDV	1	Development of military shadows on CXR	Hospitalization, TB Px prolonged to 12 m
5	F	20	13	3TC, d4T, IDV	1	Increased right upper lobe shadow	Hospitalization
6	F	39	147	AZT, ddI-EC, EFV	3	Development of new cervical lymph node	Steroid therapy, TB Px prolonged to 14 m
7	M	31	30	TDF, FTC, Kaletra	1	Increased bilateral lung shadows, pleural and pericardial effusion	Hospitalization, ART discontinued
8	F	48	100	3TC, d4T, LPVr	3	Increased cervical and mediastinal lymph node, development of pelvic abscess	Hospitalization, incision and drainage, TB Px prolonged to 15m
9	M	41	62	3TC, ABC, d4T, LPVr	1	Development of pericardial effusion without cardiac tamponade	Hospitalization, steroid therapy, ART discontinued, Px prolonged to 12 m

CBV: combivir; **IDV**: indinavir; **3TC**: lamivudine; **AZT**: zidovudine; **d4T**: stavudine; **ddI-EC**: Videx EC; **EFV**: efavirenz; **TDF**: tenofovir; **FTC**: Emtricitabine; **LPVr**: lopinavir co-formulated with ritonavir; **ABC**: abacavir

Conclusions

Early initiation of HAART is associated with favourable TB treatment outcomes in patients with HIV-associated TB. The better treatment outcome in this group of patients suggested that negative effect due to adverse effects from drugs and IRIS brought about by early initiation of ART was offset by the restoration of immune function. HAART should be started early during the course of anti-TB treatment for patients with HIV-associated TB.

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