

Incidence and Risk Factors for Tenofovir-associated Renal Function Decline among Thai HIV-infected Patients with Low-body Weight

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Introduction

- Tenofovir (TDF) is recommended as one drug of the preferred antiretroviral regimen for the treatment of HIV infection
- Nephrotoxicity attributable to TDF have been published, such as Fanconi syndrome, nephrogenic diabetes insipidus, increase creatinine level, and acute renal failure
- Incidence, including risk factors, for TDF-associated nephrotoxicity in routine HIV clinical care settings have not been well established
- Scanty information in Asian HIV-infected patients, who have lower body weight, has been reported
- We aimed to determine the incidence and risk factors for TDF-associated renal function decline, defined by 25% decrease in glomerular filtration rate (GFR)

Method

- Retrospective and prospective cohort studies, between January 2007 and October 2009
- HIV-infected patients who attended the HIV clinic at Chonburi Hospital (an 825-bed tertiary care hospital)
- Inclusion criteria; (1) age ≥ 18 years old, (2) received normal dose of TDF ≥ 3 months, (3) had information on baseline weight and serum creatinine, and (4) had baseline GFR > 50 ml/min/1.73m²
- GFR was calculated by using the Simplified Levey modification of diet in renal disease (MDRD) formula
- Exclusion criteria: (1) received concurrent indinavir, and (2) did not have at least one follow-up visit

Table 1 Baseline characteristics and laboratory investigations at tenofovir initiation of 405 patients

Characteristics	Total N=405	No 25% decrease in GFR N=327	25% decrease in GFR N=78	P-value
Median (IQR) age, years	40 (36-45)	40 (36-45)	38.5 (34-44)	0.104
Male gender, n (%)	230 (56.8)	189 (57.8)	41 (52.6)	0.402
Experience to antiretroviral, n (%)	401 (99)	325 (99.4)	76 (97.4)	0.169
Median (IQR) body weight, kg.	56.5 (50.5-65.0)	57 (51-65)	55 (49-63)	0.063
Body weight < 60 kg, n (%)	244 (60.2)	190 (58.1)	55 (70.5)	0.044
Underlying disease, n (%)	95 (23.5)	79 (24.2)	16 (20.5)	0.446
Hypertension	38 (9.4)	33 (10.1)	5 (6.4)	0.316
Hepatitis B and/or hepatitis C	36 (8.9)	29 (8.9)	7 (9.0)	0.976
Diabetes mellitus	21 (5.2)	17 (5.2)	4 (5.1)	1.000
Concurrent nephrotoxic drug, n (%)	49 (12.1)	34 (10.4)	15 (19.2)	0.032
Median (IQR) CD4 cell counts, cells/mm ³	352 (220-507)	353 (221-514)	345 (205-503)	0.498
Median (IQR) duration of ART before TDF initiation, month	48 (24-72.7)	48 (24-72.5)	48 (24-72)	0.958
ART regimen				0.144
NNRTI-based, n (%)	287 (70.9)	237 (72.5)	50 (64.1)	
PI-based, n (%)	118 (29.1)	90 (27.5)	28 (35.9)	
Median (IQR) baseline SCr, mg/dl	0.9 (0.8-1.0)	0.9 (0.8-1.0)	0.8 (0.7-0.9)	<0.001
Median (IQR) baseline GFR, ml/min/1.73m ²	85.8 (75.0-97.1)	87.8 (76.7-99.4)	100.9 (88.9-102.2)	<0.001

SCr, serum creatinine, GFR, glomerular filtration rate, IQR, interquartile range, NNRTI, non-nucleoside reverse transcriptase inhibitor, PI, protease inhibitor, SD, standard deviation, TDF, tenofovir

Table 2 Associated factors for tenofovir-associated renal function decline by 25% decrease in glomerular filtration rate from the baseline

Variables	Logistic regression			
	Univariate		Multivariate	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Underlying disease	0.79 (0.42-1.46)	0.446	-	-
Male gender	0.81 (0.49-1.33)	0.402	-	-
Baseline CD4 cell counts, per 100 cells/mm ³	0.94 (0.84-1.07)	0.358	-	-
Age, per year	0.97 (0.94-1.01)	0.105	-	-
Duration of antiretroviral therapy before TDF initiation, per month	1.00 (0.99-1.00)	0.923	-	-
Body weight, per 5 kg decrement	1.14 (1.00-1.30)	0.047	1.15 (1.00-1.33)	0.043
Protease inhibitor-containing regimen	1.48 (0.88-2.49)	0.145	2.12 (1.15-3.92)	0.016
Baseline GFR, per 10 ml/min/1.73m ²	1.55 (1.34-1.79)	<0.001	1.62 (1.39-1.88)	<0.001
Concurrent nephrotoxic drug	2.05 (1.05-3.99)	0.034	3.16 (1.44-6.98)	0.004

Results

- A total of 405 HIV- patients were eligible for the analysis
- Summary of patients' characteristics is shown in Table 1
- Median (IQR) duration of receiving TDF was 16 (8-21) months
- 78 (19.3%) patients had 25% decreases in GFR from the baseline, incidence rate of 16.2 per 100 person-years
- By Kaplan-Meier survival analysis, median time to 25% decrease in GFR was 28 (95% CI 25.2-30.8) months
- Statistical significance of the overall changes in median GFR over time after TDF initiation (P < 0.05) (Figure 2)
- Renal function of 28 patients is reversible after dose adjustment or discontinuation
- By multiple logistic regression, lower body weight (OR 1.15 per 5 kg, 95% CI 1.00-1.33, P=0.043), baseline GFR (OR 1.62 per 10 ml/min/1.73m², 95% CI 1.39-1.88, P < 0.001), protease inhibitor (OR 2.12, 95% CI 1.15-3.92, P=0.016), and concurrent nephrotoxic drug (OR 3.16, 95% CI 1.44-6.98, P=0.004) were statistically significant associated with 25% decreased in GFR after adjusting other factors

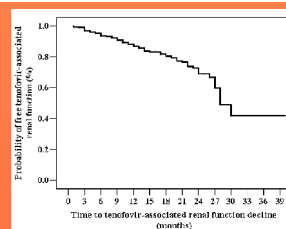


Figure 1 Kaplan-Meier estimates the time to tenofovir-associated renal function by using MDRD formula

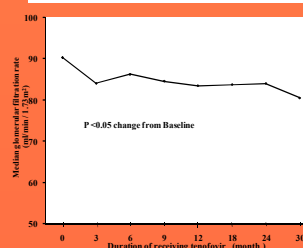


Figure 2 Changes of median glomerular filtration rate by MDRD formula over time after receiving tenofovir

N 485 273 215 174 284 177 95 29