NOVEL BIOMARKERS AND SUBCLINICAL RENAL DYSFUNCTION IN HIV PATIENTS

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Introduction and Aims

Patients with HIV have substantially elevated risk to development renal disease due to several factors related to combined antiretrotival therapy (cART), direct effect of HIV viral proteins on the glomerulus and the tubule, HIV-associated immunecomplex glomerulonephritis and chronic kidney disease (CKD)-related risk factors. Early detection of renal dysfunction is of huge importance to prevent further kidney damage in HIV patients. The aim of this study was to investigate traditional and novel biomarkers of kidney diseases in HIV patients receiving cART.

Methods

This is a cross-sectional study of HIV-infected patients recruited from public health centers in Fortaleza city, Northeast of Brazil between January and December 2015. Standard biochemical analysis in serum and urine samples was performed using a routine automated analyser. Urinary osmolality was determinated in a vapor pressure osmometer. GFR was estimated using MDRD Equation. Urinary albumin and urine protein concentration were expressed as ratios to urinary creatinine concentration, uACR and uPCR, respectively. Urinary MCP-1 (uMCP-1), KIM-1 (uKIM-1), NGAL (uNGAL) and serum NGAL (sNGAL) levels were determined using a commercially available ELISA kit. The assays were performed according to the manufacturer's instructions. Each sample and standards were tested in duplicate. The urinary biomarkers were expressed as values corrected by the urinary creatinine concentrations.

Results

Table 1. Renal parameters of HIV-infected patients according to cART use and comparison with control group.

	Control (n=13)	No cART (n=18)	cART/Tenofovir (n=27)	cART/Zidovudine (n=21)	*P* value
Renal parameters					
UpH	5.7±0.2	5.7±0.4	5.7±4.7	5.8±4.1	0.703 [a]
Uosm(mOsm/Kg)	962±155	720±198*	762±250	734±243*	**<0.05** [a]
Uosm/Posm	3.4±0.7	2.4±0.7*	2.6±0.8*	2.5±0.9*	**<0.05** [a]
sNa (mEq/L)	138±3	140±2,5	139±1,8	138±1,3	0.239 [a]
sK (mEq/L)	4.2±0.3	4.4±0.5	4.2±0.4	4.3±0.3	0.723 [a]
EF_{Na} (%)	0.46±0.25	0.58±0.27	0.55±0.28	0.74±0.35*	0.045 [a]
uGlucose (mg/dL)	5.9±2.6	5±3.1	4.6±2.7	4.5±1.6	0.424 [a]
sCreatinine (mg/dL)	0.57±0.2	0.60±0.13	0.63±0.2	0.63±0.14	0.704 [a]
sUrea (mg/dL)	24.7±5.3	25±6.2	23±7.6	24.5±6	0.741 [a]
eGFR (mL/min/1.73²)	166±67	140±32	140±41	138±36	0.274 [a]
uPCR (mg/g-Cr)	51.7±22	53.5±26	77.5±46	58.4±27.5	0.085 [a]
uACR (mg/g-Cr)	3.9 (1.3 – 5.6)	3.8 (0.7 – 4.2)	3.7 (1.3 – 6.0)	1.8 (1.0 – 5.0)	0.909 [b]

Data are presented as the mean ± standard deviation or as median (interquatile range).
* $p < 0.05$ compared with control group.

Table 2. Novel biomarkers of kidney dysfunction in HIV-infected patients according to cART use and comparison with control group.

	Control (n=13)	No cART (n=18)	cART/Tenofovir (n=27)	cART/Zidovudine (n=21)	*P* value
uMCP-1 (pg/mg-Cr)	26.9 (13 – 53)	68.5 (31 – 180)*	65.8 (36 – 95)*	62.6 (49 – 152)*	0.012
uNGAL (ng/mg-Cr)	3.6±2.5	6.7±6.6	3.3±2.7	4.3±3.9	0.075
sNGAL (ng/mL)	102.4±28.8	103.5±24.9	117.6±32.5	114±41.2	0.417
uKIM-1 (ng/mg-Cr)	0.70±0.2	-	1.25±0.6*	-	<0.001

Data are presented as the mean ± standard deviation or as median (interquatile range).
* $p < 0.05$ compared with control group.

Figure 1.a. Median and interquatiles range (IQR) of urinary monocyte chemotactic protein-1 (uMCP-1) in control and HIV-infected patients.

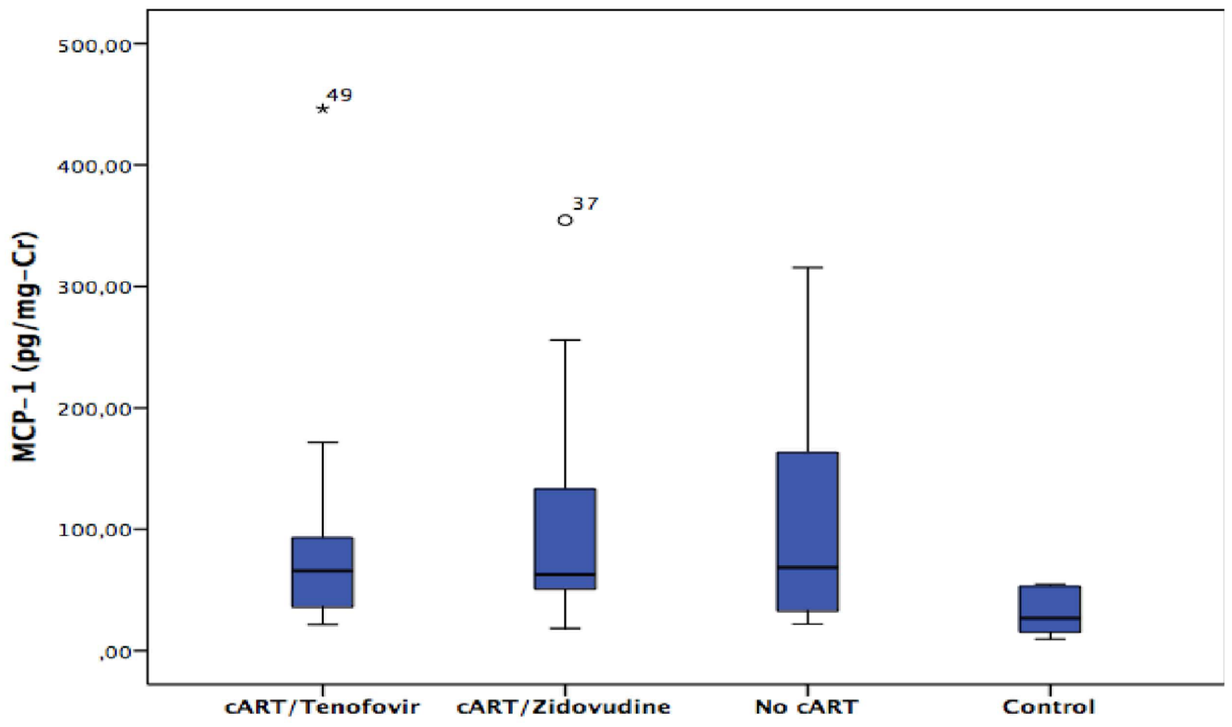
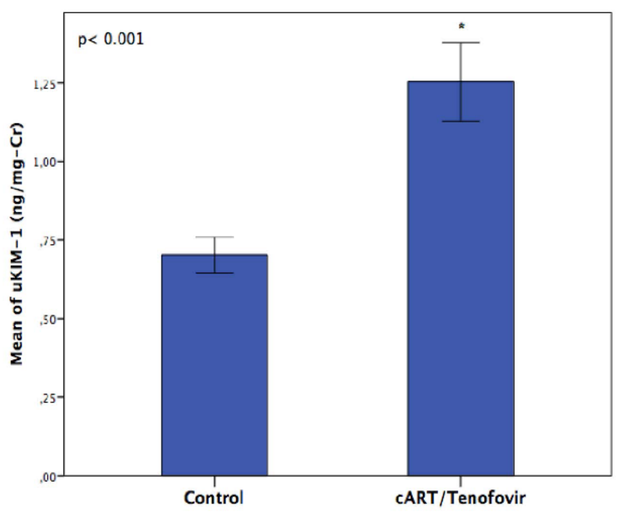


Figure 1.b. Means of urinary kidney injury molecule-1 (uKIM-1) in controls and HIV patients using tenofovir in cART.



Conclusions

Important subclinical kidney damage using uKIM-1, uMCP-1 and abnormalities in urinary concentrating capacity and sodium excretion fraction (EF_{Na}) were detected among HIV patients. HIV patients in chronic use of cART presented subclinical renal damage and elevated uKIM-1 in patients using tenofovir.

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