Reviewer's report

**Title:** Total protein, albumin and low-molecular-weight protein excretion in HIV-positive patients

**Version:** 2  **Date:** 28 February 2012

**Reviewer:** MINORU ANDO

**Reviewer's report:**

**Major concerns:**
This study showed prevalence of proteinuria and albuminuria, and urinary concentrations of LMWPs including RBP, cystatin C and NGAL as markers for subclinical tubular dysfunction or structural damage. They were also compared among 4 groups, that is, groups receiving no cART, cART/no TFV, TFV/NNRT and TFV/PI. The results could be lack of novelty. Numerous articles have already reported prevalence (extent) of proteinuria and albuminuria in multiethnic HIV populations, with special reference to cardiovascular disease and mortality. The authors likely want to emphasize that RBPCR could be a potential marker for early renal tubular injury in HIV-infected individuals receiving cART/TFV. However, similar significance of the urinary concentrations of LMWPs including RBP has been suggested in the HIV-infected individuals with incipient glomerular defects by Kabanda A et al (AJKD 27; 803-8, 1996) and Hall AM et al (AJKD 54; 1034-42, 2009). In addition, Ando M et al studied prevalence of tubular damage in the absence of apparent glomerular defects in HIV-infected patients on HAART using multiple urinary concentrations of LMWPs, and showed clinical associations of tubular damage with a near-term decline in eGFR and higher incidence of proteinuria (NDT 26; 3224-29, 2011). This paper is rather descriptive in nature, and thus it is unclear whether the data shown is clinically significant or simply epiphenomena with comorbidities including CKD, diabetes, and hypertension.

**Minor concerns:**
1. Nobody can determine that individuals with upper quartile RBPCR have proximal tubular injury without renal biopsy findings or tubular functional tests.
2. Readers may want to know the reference values for urinary concentrations of NGAL, cystatin C and RBP to see that they are elevated or not in the HIV cohort.
3. Readers may want to see the data on dipstick test for proteinuria.
4. The reviewer wonders why you took the value of eGFR <75 ml/min/1.73 m2 as a cutoff value?
5. Duration of cART (especially TFV) and cumulative use of other nephrotoxic drugs should be clarified.
6. Habit of smoking and drugs should be considered as well.
Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.