Author’s response to reviews

Title: PREDICTIVE FACTORS AND PREVALENCE OF MICROALBUMINURIA IN HIV-INFECTED PATIENTS: A CROSS-SECTIONAL ANALYSIS

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Reviewer reports:

Sana Waheed (Reviewer 1): This study addresses an important question of the prevalence of proteinuria in the HIV population and the study is designed to address that.


Despite the fact that ACR and albuminuria in a 24 hour urine collection are the gold standard tests, we have chosen to evaluate the microalbuminuria dosage on a single spot urine collection, since we were looking for a simple, easy-to-use and cheap method. As a consequence, being
aware of the possibility of loss in accuracy, we decided to use a lower cut-off and to have a two-samples analysis in order to decrease the diagnosis underestimation and overestimation, respectively.

2) The LDL levels changed significantly in the subgroups over time and is there any physiologic explanation for that?

We do not believe that there could be a physiologic explanation for this variation (the mean variation in the “equal” group is 2.9 mg/dL; in “improved” group is 22.2 mg/dL and in the “worse” group is -3.7 mg/dL). These values are statistically significant but we believe that the variation there isn’t clinical significance.

3) The potential utilization of cystatin C in the HIV population as a better marker of GFR than creatinine is indeed an exciting concept however, the data presented does not support that conclusion. However the study does show correlation of cystitis C levels and microalbuminuria which was highlighted by the authors.

We modified the text as follows:

“We noticed an increase in Cystatin C in all the patients after a 48 weeks observational period and this could relate to a worsened inflammatory state and an increased cardiovascular risk. Yet, the “worse” group shows a more pronounced increase (even if not statistically significant), presumably because of a coupled increase in microalbuminuria and a worsened renal function.”

4) The relationship of TDF use and microalbuminuria is an important one as mentioned by the authors.

In table 1 we report the statistical significant association between TDF use and microalbuminuria. In “worse” group the percentage of TDF use is significant higher (71.4%).
Denyse Thornley-Brown, MD (Reviewer 2):

Summary:

The purpose of this study was to: (1) evaluate the prevalence of microalbuminuria in a cohort of HIV positive patients; and (2) to assess the association of microalbuminuria with different therapeutic regimens.

The authors studied 326 unselected sequential patients receiving HIV care at time 0 and 48 weeks, measuring urinary microalbumin concentration as well as a number of metabolic and demographic parameters and therapeutic regimens.

Major criticisms:

1. The authors conclude that "We showed a very high prevalence of microalbuminuria, much higher than the literature data. . . "; however, the authors use an unconventional definition of microalbuminuria, i.e., "a urinary albumin excretion rate(sic)greater than 1 mg/L." While it is possible to measure such a low concentration of microalbumin, the generally accepted cut-off concentration for clinically significant microalbuminuria is higher (e.g. The cutoff used in reference 6 [Glassock] was a microalbumin concentration of 3-30 mg/dL).

Aim of the study was to have an early evaluation of renal function impairment, through a method that is cheaper, simpler and easier to use compared to the gold standard tests. Being aware of the possibility of loss in accuracy, we decided to use a lower cut-off and to have a two-samples analysis in order to decrease the diagnosis underestimation and overestimation, respectively

2. The authors compare baseline to 48 week microalbumin outcomes and divide the population into three groups: Equal, Improved and Worse. In the Equal group, microalbumin concentration remained constant at 1.2 mg/L at 0 and 48 weeks; in the improved group it went from 1.5 mg/L to 0 mg/L, and in the worse group from 0 mg/L to 1.5 mg/L at 0 and 48 weeks, respectively. While these values are statistically significant, I would question their clinical significance, especially given that the serum creatinine concentration was unchanged at 48 months and the change in cystatin C concentration at 0 and 48 months was no different between the three groups.
It would also be helpful in interpreting the data to know the coefficient of variance for the assay used.

A statistically significance of the variation is determinate by lower variability of microalbumin values. Interquartile range (IQR) show that at 48 weeks all patients in “improved” group had 0 as value of microalbumin such as at baseline all patients in “worse” group had 0 as value of microalbumin.

3. Since the outcome variable used was urinary microalbumin concentration (as opposed to microalbumin to creatinine ratio), the authors should address the issue of differences in hydration (i.e., urinary osmolality) between 0 and 48 weeks as a limiting factor in the interpretation of their results.

We did not show the data, but all the patients had a simultaneous measurement of the urinary specific gravity, so that we could highlight differences in hydration that could affect the results.

We added among the exclusion criteria: “out of range urinary specific gravity values”.

4. The authors compare the prevalence of microalbuminuria in their study to those of three other studies (references 20-22); however, these studies were in children and this manuscript is looking at an adult population.

We added the following, more relevant, references:


Minor criticisms:

1. I could not find definitions for the abbreviations used in Table 1 (specifically omo, TD, entero).

   We modified the text.

2. The majority of patients infected with hepatitis C had stable or improved proteinuria. How many received treatment for their hepatitis C during the course of the study?

   We added the following statement in the text: “No HIV-HCV coinfected patients received an anti-HCV therapy during the study period”