Author’s response to reviews

Title: Effects of ethnicity and CD4 count on glucose metabolism among HIV patients on highly-active antiretroviral therapy (HAART)

Authors:

Ranjita Misra (ramisra@hsc.wvu.edu)
Prakash Chandra (pchandr@emory.edu)
Shivani Shinde (sshinde@illinois.edu)
Dorothy E Lewis (Dorothy.E.Lewis@uth.tmc.edu)
Henry Pownall (hpownall@bcm.edu)
Ivonne Coraza (coraza@bcm.edu)
Raj V Sekhar (rsekhar@bcm.edu)
Ashok Balasubramanyam (ashokb@bcm.edu)
Steven E Riechman (sriechman@hlkn.tamu.edu)
Dustin M Long (dmlong@hsc.wvu.edu)

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To: The Editors (Attn: Eloisa Nolasco)

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Journal Editorial Office

BioMed Central

236 Gray’s Inn Road

London WC1X 8HB

United Kingdom

From: Ranjita Misra, PhD, CHES, FASHA

Professor & Director

Public Health Practice [MPH] Program

Department of Social & Behavioral Sciences
Dear Editors:

We appreciate the careful re-review of our revised manuscript “Association of ethnicity and CD4 count on glucose metabolism among HIV patients on highly-active antiretroviral therapy (HAART)” and reviewer’s constructive critiques. We have addressed all of their queries and suggestions, and believe that the manuscript is improved as a result.

Below are our specific responses to each of the reviewers’ comments.

REVIEWER 1

Minor

1. I agree that limitations can be taken in a pejorative manner. I believe that while studying only patients with hypertriglyceridemia is not a design flaw, it does limit the generalizability of the study to only patients with hypertriglyceridemia, perhaps 30% of patients. This really should be pointed out to readers to help the clinical utility of the manuscript.

RESPONSE: The reviewer’s comment is very well taken. We have added the limited generalizability of the results in the discussion section as stated below.

“The design of this study makes it difficult to specify the reasons for the relationships between ethnicity, CD4 counts and glucose tolerance in these patients. Strictly speaking these results may be generalizable to only to HIV patients with hypertriglyceridemia, however such patients comprise a large proportion of those with HIV infection on various forms of antiretroviral therapy.”

REVIEWER 2

No new comments

REVIEWER 3
Major

1. Limitations of the study are not sufficiently explained, i.e. cumulative exposure to ARV classes and to single drugs are not reported and, consequently, not included in multivariate analyses.

RESPONSE: Limitations of the analysis include the fact that not all ART drug classes or single drugs that could possibly affect insulin sensitivity were included in the multivariate analyses. However, drugs of the protease inhibitor class (which are the most strongly associated with both insulin resistance and defects in glucose uptake) were taken into consideration (i.e., use of PI was controlled for in the analyses).

2. I do not know SPSS result reports, but using other statistical software packages (like STATA) interactions between categorical and continuous variables are reported as:

   category1*continuum (or other category variable)
   category2*continuum (or other category variable)

Authors reported interactions between ethnicity and FBS (table 2a) and CD4 (2b) in one single raw. In my opinion, this is confusing and readers cannot well understand the role of AA and/or Hispanic ethnicity with high or low CD4 category.

RESPONSE: SPSS output does not provide details of the interactions like STATA. We understand it could be confusing to the reader; interactions were described in the results section.

3. One more concern is about collinearity between variable outcomes and covariates. I apologize with authors for not having mentioned this in my previous referee. In my opinion fasting glucose and HOMA-IR (table 2a) are highly related because glucose is included in the formula, and therefore this is not a variable to include in the analysis. The same problem was present in table 2b where insulin was included as covariate. Could the authors perform a collinearity test before to include variables in the model? Did the authors perform a postestimation analysis after modeling?

RESPONSE: The reviewer is correct about collinearity between HOMA-IR and
glucose in the model. The authors had tested collinearity of outcome variables and covariates prior to the multivariate analysis using a correlation of more than 0.5 as an indicator of collinearity and found that to be not an issue. For example Pearson’s correlation between glucose and HOMA-IR was $r=0.31$ and insulin was 0.229 respectively; hence they were included in the model.

On behalf of myself and my coauthors, I thank you in advance for your consideration and look forward to hearing from you.

Sincerely,

Ranjita Misra