Reviewer’s report

Title: Insulin Resistance and Adipokines serum levels in a Caucasian Cohort of HIV-positive Patients Undergoing Antiretroviral Therapy: a cross sectional study

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Reviewer: Ole-Petter Hamnvik

Reviewer’s report:

This study by Arama et al. aims to investigate the prevalence of insulin resistance in a population of 89 HIV-infected individuals taking antiretroviral therapy, and to investigate whether there is a correlation between insulin resistance and adipokine levels.

The study asks a relevant question supported by the discussion in the background section of the manuscript – are adipokines mediators of the increase in metabolic complications seen in patients with HIV on antiretroviral therapy? The study design is cross-sectional, with the associated limitations including an inability to prove causality, but certainly hypothesis-generating. The findings are hardly novel, but extends prior findings to the population studied.

The main limitation of the study is the small number of participants. With 89 participants, factors with small effects may not reach statistical significance. For example, I believe that the difference in age and BMI in patients with and without insulin resistance would be significant had the numbers been higher – affected patients being older and with a higher body mass index. The authors briefly acknowledge this limitation.

I am also not certain that confounding has been handled in an appropriate way, as the authors do not correct for age and BMI in their regression models. Hence, it is uncertain whether the people with insulin resistance are more obese and therefore have altered adipokine levels, or if their levels are different even after accounting for BMI.

Discretionary revisions:
- I would discourage the use of “complex” antiretroviral therapy. All HIV therapy is complex, and the commonly used terminology is simply “antiretroviral therapy”.

Minor essential revisions:
- I would recommend defining the QUICKI cut-off point in the abstract.
- Also define the abbreviation IR in the abstract.
- Please clarify that p-values used are two-tailed.
- The authors state that the effects of ART are acute as they are not associated with duration of therapy. As all participants had taken ART for at least 6 months, I would clarify this statement.
- Page 3: Please change “hypertrigliceridemia” to “hypertriglyceridemia”. Also
change “associates with” to “is associated with”.
- Page 7: Change typographical errors: “observed” rather than “observed”, “type 2” rather than “type II”, “regression” rather than “regresion”.
- Page 8: Change “surogate” to “surrogate”.

Major compulsory revisions:
- I would include the incidence of insulin resistance using HOMA-IR also.
- The authors claim to be giving the interquartile range for non-normally distributed variables in their table. However, they are only supplying a single number in the parentheses. I would recommend changing to median (25th percentile – 75th percentile). For example, 23.8 (21.0 – 30.2).
- In Table 1, I would include an initial column with the overall characteristics of the population.
- We also need a bit more information about the population in terms of baseline prevalence of metabolic risk factors, such as hyperlipidemia, hypertriglyceridemia and hypertension (all as categorical variables in addition to the continuous variables already presented).
- The authors are not including age or BMI in their regression model, but this is a must as both of these are known confounders between adipokines and insulin resistance. Hence, although these variables do not reach significance due to the modest n, including them is essential in order to make appropriate conclusions. Also, the women in the study are younger, could this explain the different findings between the genders?
- The authors are suggesting screening for insulin resistance in their conclusion. However, though their data shows a high incidence of insulin resistance, there is no evidence that there is any benefit in screening for insulin resistance per se. I would agree that it is necessary to screen for metabolic complications of ART, such as diabetes mellitus, hyperlipidemia and hypertriglyceridemia, and hypertension, but that is not the focus of this paper. Would recommend removing this recommendation.
- Would expand on the limitations imposed by study design and number of participants.
- The correlations seen are small to moderate in magnitude, and this should be mentioned in the paper.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

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