Reviewer's report

Title: Reduced IgM Levels and Elevated IgG Levels against Oxidized Low-Density Lipoproteins in HIV-1 Infection

Version: 2 Date: 24 January 2014

Reviewer: Theodoros Kelesidis

Reviewer’s report:

The study lacks significant novelty since the levels of oxLDL antibodies have previously been determined in HIV infection. In addition, the findings that these antibodies are higher in HIV patients are not unexpected since HIV patients have hypergammaglobulinemia and polyclonal B cell activation and as the authors mention “there is a higher activity of the humoral immune system in these individuals” so in theory any different type of antibodies that are measured in HIV patients are higher than negative controls. They just confirm an association of HIV with inflammation and higher levels of certain antibodies and the findings are not well linked to the research question on how this is pertinent to the pathogenesis of HIV atherosclerosis. Also B cell defects in HIV patients may explain low IgM levels of certain antibodies.

An important analysis would be to normalize the measured oxLDL IgG levels with the total IgG levels and similarly the IgM oxLDL with the total IgM levels and redo the analysis.

It would be more interesting if they also measured actual circulating levels of oxLDL and looked at certain measurements of atherosclerosis e.g. CIMT etc. The story is incomplete and the manuscript gives the impression of a constellation of measurement and associations in a small study with suboptimal design due to the limited power.

There are no power analysis calculations in the methods section. The authors mention that “the size of this study is relatively small, leading to a limited power to detect some associations between biomarkers, but the study subjects are well characterized and we have a well-matched HIV control group, strengthening our findings of increased IgG levels in HIV+ individuals” This is not adequate explanation. The negative findings were most likely related to the small numbers. The study design is suboptimal to address this research question.

The rationale why certain measurements were performed is not explained adequately. “We measured ApoB and ApoA1 as potential markers of cardiovascular risk” is not an adequate explanation why this is important for this study since these have been measured previously in other studies? What was the hypothesis and how is this related to the main research question (levels of oxLDL antibodies)?

Similarly “Individuals with HIV infection have been proposed to have increased
microbial translocation,
and we therefore analyzed sCD14 and the inflammation marker proposed as a cardiovascular risk marker, CRP" is not an adequate explanation. How is this related to the main hypothesis and research question? This seems another irrelevant measurement that needs to be justified accordingly. IF the authors were interested in microbial translocation why did they measure only sCD14 (and not LPS)? In addition how do they explain the inverse correlation between circulating levels of sCD14 and total IgG and IgM, and the absence of relationship between sCD14 and specific IgG or IgM directed against OxLDL or MDA-LDL" ?

Both serum and plasma have been used in this study. What is the evidence that the data (oxLDL antibodies, levels of oxLDL) between the different matrices are comparable? IF this has not been previously published or studied the authors need to show pilot data that the data are comparable between plasma and sera. Similarly both fresh and stored samples were used in this study. Cryopreservation can significantly affect levels of oxidized lipids including oxLDL. How are the results ((oxLDL antibodies, levels of oxLDL) comparable between fresh and frozen samples?

Minor comments
Correct typos throughout the manuscript e.g OLDL
“blood lipids were analyzed” Which lipids and how were they measured?

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests