Author’s response to reviews

Title: Evaluation of alterations in serum immunoglobulin concentrations in components of metabolic syndrome, obesity, diabetes, and dyslipidemia

Authors:

Dee Lin (dee.lin@rutgers.edu)

Mary Barna Bridgeman (mary.bridgeman@pharmacy.rutgers.edu)

Luigi Brunetti (brunetti@pharmacy.rutgers.edu)

Version: 3 Date: 01 Nov 2019

Author’s response to reviews:

Thank you for your review. We appreciate your comments. Please find a point-by-point response below.

GENERAL COMMENTS: This cross-sectional study analyzed the association between serum immunoglobulins (Igs) and cardiovascular risk factors such as obesity, diabetes, and dyslipidemia. The statistical analysis has been adequately performed, and the results are clearly presented. However, a major problem is that the method used for the measurement of Igs was not described in the manuscript while the data were collected from two hospitals.

Response: We did not measure Ig concentrations, nor did we have control over the choice of assay as this was a cross-sectional study. We relied on existing data. It is unlikely that the same assay was used between hospitals or consistently over the course of 7 years. We have added additional text to the manuscript to highlight this potential limitation. However, we have no reason to believe that one assay was chosen preferentially for those with or without metabolic disease. We have added to the discussion.

REQUESTED REVISIONS: The authors have basically responded to the questions of the reviewer. However, the change in the revised manuscript resulting from the response to question 1 is not sufficient for understanding how they controlled the covariates such as dyslipidemia, diabetes and, obesity. More detail for such analysis is needed.

Response: We constructed general linear models using the GLM procedure in SAS (https://support.sas.com/rnd/app/stat/procedures/glm.html). This is a standard technique to adjust the means of a variable of interest for potential confounders. We have added additional text further clarifying this concern. We have also added references supporting this strategy for selection of covariates to include in the GLM model. The primary covariates of interest were dyslipidemia, obesity, and diabetes. We then included other covariates that were determined to be possible confounders to adjust the Ig concentrations. We further clarified the text in the statistical analysis section.
The method of measuring serum immunoglobulins (Igs) was not described in the manuscript. Was the measurement of Igs done with the same method or with different methods? The presentation of values was not specified in the method section.

Response: See comment above.

In statistical analysis, what is the reason to include a bivariate P-value less than 0.2 in the GLM for all demographic and clinical variables?

Response: This is a standard technique in facilitating the selection of variables to include in the final generalized linear model. Using a p<0.2 is a conservative entry criterion into the model. It allows more variables to be entered/tested. Note that only variables with a p<0.05 were included in the final models. We provided further text in the manuscript as well as references that utilized this technique.

It remains unclear how you adjusted the measured Ig values for age, sex, race, and so on. This should be carefully described in the section of statistical analysis.

Response: As currently described in the manuscript, we used the GLM procedure to adjust Ig concentrations for potential confounders. We have further elaborated on this standard statistical technique. In addition, an adjustment is not required if the covariates do not significantly influence the endpoint. That was the reason for the bivariate analysis to first identify variables that might be confounders (or influence the Ig concentrations) and then we tested in the final model and included only if p<0.05. When constructing a model that accounts for other variables (adjusting for variables), it is not statistically correct to adjust for every variable. This results in over correction potentially confounding the results.

ADDITIONAL REQUESTS/SUGGESTIONS:
In the abstract, line 47, why are these words there?

Response: We have deleted these words.

The term of GLM should be defined in the text where it appeared for the first time.

Response: We have now defined on first use.