Author’s response to reviews

Title: The Association of Religious Affiliation with Cholesterol Levels among South Asians: The Mediators of Atherosclerosis in South Asians Living in America Study

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Author’s response to reviews:

Dear Dr. Hering:

My co-authors and I are grateful for the reviewers’ comments and your consideration of our manuscript for publication in BMC Cardiovascular Disorders. Please find below our point-by-point responses to the reviewers’ comments and suggestions. We have made revisions in the manuscript text to incorporate the changes as recommended by reviewers, and highlighted our changes in the revised manuscript as per your instructions. We have also attached the response letter as supplementary material because we could not insert the data and tables for the reviewers here.

Reviewer #1

1. The number of subjects within religious affiliations other than Hinduism/Jainism are low. These should be discussed and mentioned in the limitations.

Response: We agree that this is a clear limitation within this cohort. We have added a few sentences in the discussion section to address this limitation (page 13, lines 19-23).
2. The authors should also take into consideration that higher HDL levels in some groups might be related not to higher alcohol consumption in those groups but also to higher physical activity.

Response: Thank you for this important observation. We agree that this may be the case and have added a few sentences, as well as highlighted the existing text in the discussion section that supports this observation (page 12, lines 10-14). We did not reiterate the role of physical activity on mediating the focal association strongly because it did not reach statistical significance in the analysis. Please check the attached response letter for the STATA results of the pair-wise mediation analysis for HDL that shows that there was a significant mediation effect for alcohol but not for exercise.

3. The observed differences in LDL levels are not pronounced, not exceeding 10 mg/dL, the same in HDL levels - not exceeding 4 mg/dL. Are these differences of clinical importance? Also only the differences between Muslims and no religious affiliation reached the statistical significance.

Response: The differences of LDL and HDL between religious affiliation groups are clinically meaningful. In a meta-analysis comparing low carbohydrate diet and low-fat diet interventions for weight loss, the average increase in HDL was between 2 to 4 mg/dl and average decrease of LDL was between 2 to 6 mg/dl (1). Lifestyle change with weight loss is the first treatment option promoted for dyslipidemia by the current AHA/ACC lipid guidelines (2), so these effects are meaningful. There were significant differences in LDL between Hindus/Jains and Muslims (p=0.02) (page 10, lines 1-2; page 12, lines 10-14), and in HDL between Hindu/Jains and those with no religious affiliation (p=0.04) (page 10, lines 3-5; page 10, line 21; page 12, line 22 to page 13, line 1), in addition to the significant differences in cholesterol levels between Muslims and those with no religious affiliation. We have highlighted the text in the results section which supports this data (page 10, lines 1-5).

4. Only the conclusion "Muslims had higher LDL and triglyceride levels, and lower HDL levels, while participants with no religious affiliation had lower LDL levels and higher HDL levels." is supported by the data but not the major conclusion drawn by the authors "In conclusion, our results suggest that religion is associated with cholesterol levels in South Asians, and that some lifestyle behaviors may partially explain this risk."

Response: Thank you for bringing this to our attention. We agree that while Islam had the most apparent association with cholesterol, our study also found that Hinduism/Jainism was associated with lower HDL levels compared to those with no religious affiliation. We have highlighted the text in the results and discussion sections supporting this conclusion (page 10, lines 1-5; page 10, line 21; page 12, line 22 to page 13, line 1) and added information to Table 2. Similarly, there
were differences in cholesterol levels between different religious affiliations compared to each other (not solely compared to those with no religious affiliation) when we ran the pair-wise comparisons suggesting that this may be due to differences in lifestyle behaviors such as diet and physical exercise. For example, the difference in LDL levels between Hindus/Jains and Muslims was significant (Table 2) (page 10, lines 1-2). The South Asian religions are quite diverse in their proscriptions and diets and hence we hypothesize that those who do affiliate with a religion tend to follow the religion-specific dietary guidelines. Please see the attached response letter for STATA results for the pair-wise comparisons in the base model for HDL.

Reviewer #2

1. In the Abstract section, please use the consistent expression of data, mean±SD not median.
Response: Thank you for raising this point. In order to have a better measure of central tendency, since the distributions for HDL and triglycerides were skewed, we presented the median instead of the mean. In this cohort, the means and standard deviations for HDL and triglycerides were 50±13 mg/dL and 131±72 mg/dL, respectively.

2. Please provide cholesterol medication use according to religious affiliation. Currently, it remains unclear whether lipid lowering therapy affects the distribution of dyslipidemia according to religious affiliation. Particularly that 74% of participants belonged to one religious' affiliation, and the remaining religious groups included not more than 5-7% of participants.
Response: Cholesterol medication use did not differ significantly by religious affiliation (p=0.36) (see table below or in the attached response letter). We have added a sentence on this to the results section in the text (page 9, lines 12-13). We have shown overall cholesterol medication use in Table 1, but not categorized by religious affiliation. Additionally, while it does not necessarily confound the association between religious affiliation and cholesterol levels, we adjusted for cholesterol medication use in the models in order to alleviate bias due to this very concern.

<table>
<thead>
<tr>
<th>Religious Affiliation</th>
<th>Cholesterol Medication Use (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hinduism/Jainism</td>
<td>30.7</td>
</tr>
<tr>
<td>Sikhism</td>
<td>23.5</td>
</tr>
</tbody>
</table>
Islam 27.4
Other 28.6
None 19.6

3. Please provide data for body mass index and waist circumference. Were cholesterol levels associated with overweight and abdominal obesity? It would be clinically important to determine whether Asian living in US for approximately half of their lives become obese compared to Asian living in their original country. Currently, it has not been sufficiently justified that religious affiliation impact on lipid abnormalities.

Response: This is a great question. We focused on the association solely between religious affiliations and cholesterol levels among the South Asian community in the U.S., specifically because a prior study using the MASALA data has reported that religious affiliation was associated with overweight/obesity, as defined by BMI and waist and hip circumference, and we wanted to avoid any possible overlap with that study (3).

4. Please provide lipid data for men and women separately according to religious affiliation (Table 1). How many women were postmenopausal? This could have an impact on lipid abnormalities.

Response: We had checked for sex-specific interactions in all of our multivariable regression models, and found no evidence that sex modified the association between religious affiliation and cholesterol levels. We had briefly mentioned this in the methods section of the text (page 8, lines 21-22). The table in the attached response letter shows the mean LDL, HDL and triglycerides by sex categorized by religious affiliation. There were statistically significant differences by sex in mean HDL among Hindus/Jains, Sikhs, Muslims and other religious affiliations, and in mean triglycerides among Hindus/Jains. Overall, 65% of the women were post-menopausal. Only mean HDL showed a statistically significant difference between pre- and post-menopausal women (see below/in attached response letter).

<table>
<thead>
<tr>
<th></th>
<th>Pre-menopausal</th>
<th>Post-menopausal</th>
<th>p</th>
<th>All Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean LDL, mg/dL</td>
<td>113.7</td>
<td>114.3</td>
<td>0.858</td>
<td>114.1</td>
</tr>
<tr>
<td>Mean HDL, mg/dL</td>
<td>53.4</td>
<td>56.9</td>
<td>0.013</td>
<td>55.6</td>
</tr>
<tr>
<td>Mean Triglycerides, mg/dL</td>
<td>115.7</td>
<td>120.7</td>
<td>0.335</td>
<td>119.0</td>
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</tbody>
</table>
We thank the editors and reviewers for the helpful comments and suggestions that have improved our manuscript significantly and have made our manuscript more valuable to the readers of BMC Cardiovascular Disorders. We look forward to your decision.

Sincerely,

Grishma Hirode and Alka Kanaya

References:

