Reviewer's report

Title: Selected risk factors for atherosclerosis in children and their parents with positive family history of premature cardiovascular diseases: a prospective study

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Reviewer: Michael Mendelson

Reviewer's report:
The authors provide description of early life differences in lipid profiles, cell adhesions molecules, and carotid intima media thickness (cIMT) among those with and without a family history of premature cardiovascular disease (CVD). This is a relevant and widely applicable study. A family history of premature CVD is a strong risk factor for CVD and defining the early life manifestations that occur in relation to this risk factor can help focus screening and prevention efforts on the appropriate targets in the appropriate age group. The authors did not find a difference in the molecular assays among 137 newborns in association with the family history status. Among a subset of the participants at ~2 years of age, there was higher triglyceride-rich lipoproteins (TG, VLDL) and lipoprotein-a, but not cIMT, among those with a family history premature CVD. Confirming previous studies, the authors describe differences in serum lipids depending on maternal pre-pregnancy BMI and birthweight. The authors also provide inter-marker correlations.

The major concern for this manuscript is a complete lack of description of the statistical methods used in the analyses. It is impossible to determine the appropriateness of the analyses without knowing what was done.

Additional comments:
1) Abstract - The authors conclude that IMT is not a reliable measure of atherosclerosis in young children. Their study did not assess this. They only found that IMT does not differ in a small group of children based on family history status. This is unsurprising as even in Familial
Hypercholesterolemia with markedly elevated LDL, cIMT differences can only be observed as young as 8-10 years of age.

2) Background (Pg 3 In 39) - The authors state that obesity is not a risk factor for atherosclerosis in the Framingham Heart Study. This is incorrect as stated. BMI does not remain as an independent predictor in a prediction model when including other BMI related factors (lipids, BP, DM) but it is nonetheless a risk factor for atherosclerosis.

3) Background - Overall, the background is too long and covers much that is tangential to this study.

4) Methods - Provide some description of the recruitment strategy for participants. Was there selection bias?

5) Methods - Pg 5 In 34 - Should be 18 to 30? not 18 to 3?

6) Methods - How did the participants that came for the second stage differ from the overall group?

7) Methods - A diagram of the study design may be helpful in understanding what was done, on whom, how many, and at what time points.

8) Methods - as stated above, there is no description of the statistical analysis

9) Methods - why is birthweight categorized and not examined as a continuous variable?

10) Results - The primary analyses as stated in the title and text is the comparison between family history positive and negative. The birthweight and maternal pre-pregnancy BMI appear secondary analyses. If so, the results could be organized more clearly.

11) Results - the inter-marker correlation would be better presented as a half matrix table.

12) Discussion - The rationale for why the lp(a) differs in the smaller older children subset and not the larger newborn subset is not clearly explained in the discussion (page 10, ln 1-10)

12) Discussion - no correction for multiple testing should be listed as a limitation

13) Some very minor grammatical errors throughout.

**Are the methods appropriate and well described?**

If not, please specify what is required in your comments to the authors.

No
Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.
Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.
No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.
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