Author’s response to reviews

Title: Quantitative pedigree analysis and mitochondrial DNA sequence variants in adults with cyclic vomiting syndrome.

Authors:

Thangam Venkatesan (tvenkate@mcw.edu)
Nilay Kumar (nikumar@mcw.edu)
Jyotirmoy Sengupta (rsengupta@nrconsults.com)
Muhammad Ali (muhammad.ali@phhs.org)
Baber Malik (babermmalik@gmail.com)
Aniko Szabo (aszabo@mcw.edu)
Miranda A.L. van Tilburg (tilburg@med.unc.edu)
Essam A. Zaki (ezaki@chla.usc.edu)
Richard G. Boles (rboles@chla.usc.edu)

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Author’s response to reviews: see over
Dear Dr. Morawska,

We would like to thank the reviewers for their insightful and thoughtful comments. We have made revisions as suggested and a point-by-point response is provided below. The corrections have been highlighted in yellow for the convenience of the reviewers.

Reviewer’s report:

Discretionary Revisions

1. The terms ‘CVS plus’ and ‘catamenial’ appear in a table but (?) are not mentioned or referenced in the text.

We have included this in the background and have provided appropriate references.

2. The very high percentage of CVS patients having surgery perhaps deserves comment.

We had omitted commenting on this to avoid digressing from the main objective of our study. We agree that this is an important finding and have included this in the “results” and “discussion section”.

Editorial comments:

3. The authors investigated 2 SNPs already being known. Is there any knowledge about other mt SNPs that could contribute to the clinical manifestation of CVS. If yes, this should be discussed in detail. Furthermore, the authors should clearly limit their findings to these SNPs and discuss the possibility that other variations (even not identified yet) might contribute as well.

There are no reports of any other mtSNP’s that are associated with CVS currently and both due to the prohibitive cost of sequencing the entire mitochondrial genome ($ 20,000 /sample) as well previous literature in children identifying only these two SNP’s, we chose to restrict our analysis to the stated SNP’s.

We have alluded to the possibility of other unknown mtDNA SNP’s that may be contributing in the second paragraph of the discussion section.

“However there was no correlation between the patterns of inheritance and mtDNA SNP’s 16519T and 3010A as expected; this could be explained by the presence of yet unidentified mitochondrial polymorphisms beyond the two that were studied. While DNA methylation may be another possible explanation this would be less likely and needs to be explored in future studies.”
4. The authors need to check the manuscript carefully for simple mistakes (e.g. SNP?s, missing /additional spaces at commas or dots)

Corrections made

5. The 17-fold odds ratio (background) needs to be linked to publication(s)

Correction made

6. Check and correct table 1 concerning exact numbers (race and prophylactic medications are not correct; sum-up does not lead to available n of raw 2.)

Correction made

- the table did not copy correctly and as a result some of the rows under race were hidden. We have corrected this as well a typographical error under prophylactic medications. Available data ( n ) is included in the table

7. Since citation is done by numbers and superscript (1), use other symbols for identifying statistical tests in table 1 and 2; stay consistent concerning these symbols in legends and tables

Correction made

Executive Editor: 1) Please spell out the full names of the ethics committees that approved your study.

Correction made

Sincerely,

Thangam