Reviewer’s report

Title: TRMA syndrome with a severe phenotype, cerebral infarction, and novel compound heterozygous SLC19A2 mutation: a case report

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Reviewer: RB Ashokkumar

Reviewer's report:

Title: TRMA syndrome with a severe phenotype, cerebral infarction, and novel compound heterozygous SLC19A2 mutation: a case report

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This manuscript presents a case report from Chinese origin with TRMA syndrome, an intriguing genetic disorder of thiamin deficiency, where two novel mutations such as c.405dupA (p.Ala136Serfs*3) and c.903delG (p.Trp301Cysfs*13) were diagnosed in compound heterozygous state in the high affinity thiamin transporter SLC19A2. Substantial clinical data is also provided to understand the complications associated with this syndrome. Moreover, this study has recorded remarkable recovery of the proband with respect to most of the disease associated symptoms upon thiamin supplementation. This manuscript is generally well-written, methods are current and reasonable. However, few concerns have been raised and can be addressed and modified by the authors accordingly. I recommend revising this manuscript with minor changes before its acceptance for publication.

Major Comment:

1. This study has documented two novel mutations such as c.405dupA (p.Ala136Serfs*3) and c.903delG (p.Trp301Cysfs*13) in compound heterozygous state in the TRMA patient. Further, authors have stated that c.405dupA mutation has been inherited from father and c.903delG mutation has been inherited from mother. But, it is not correctly presented in the Figure 2 and it looks like the chromatograms of father and mother are switched over. Authors can check for this and correct it.

2. Authors can include the data reg the status of these mutations from the healthy volunteers (atleast 50) of same ethnic group if available.
Minor Comments:

1. In the discussion, authors have mentioned that there are only 40 mutations in SLC19A2 have been reported from TRMA patients. According the HGMD database, 45 mutations are documented in the SLC19A2 gene from TRMA patients. Thus, the authors can include this update in the revised manuscript by citing HGMD database.

2. Secondly, it is written as 'Most of these mutations are nonsense mutations', in the line no. 18, Page no. 10. This is not true......It should be corrected as 'Most of these mutations are missense/nonsense mutations'.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

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.

Not relevant to this manuscript

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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