Reviewer’s report

Title: Clinical course, mutations and its functional characteristics of infantile-onset Pompe disease in Thailand

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Reviewer: Deeksha Sarihyan Bali

Reviewer's report:

Clinical course, mutations and its functional characteristics of infantile-onset Pompe disease in Thailand is a well thought of manuscript with an objective of examining clinical and molecular characteristics of infantile-onset Pompe disease majorly in Thailand and in some other countries from that region. This paper would definitely add more to the knowledge of IOPD and molecular findings seen in the region there. However, there are some major and minor revisions needed to the manuscript, as below:

1. The major issue is with wrongly written GAA variant in their list of novel variants. This is a major typo mistake starting from abstract and continues into introduction; c. 2065G>A (pseudodeficiency allele) does not result in protein change p. D513G in exon 10. C.1538G>A is the correct nucleotide change here. They corrected this mis-calculation lateron in the manuscript but failed to read the mistakes in abstract and introduction section. Protein change associated with this nucleotide change is p. Glu689Lys in exon 15. Please check carefully and do the needed corrections.

2. This variant p.513 variant may not be a novel variant, it has been seen and published before it seems. Please check again.

3. May be a good idea to write Amino acid change in 3 letter codes throughout the manuscript rather than single Amino Acid letters for clarity and easy to follow for readers. Single letter codes get hard to follow and mistakes happen.

4. Grammatical errors in abstract and introduction (line 58 - GAA gene was analyzed). Likewise there are quite a few grammatical errors throughout the manuscript, please read it carefully.

5. Write full word for abbreviation CRIM - where it is used the first time (abstract and background).

6. GAA has 20 exons but only 19 exons are coding exons (initiation codon in exon2) and get sequenced usually using Sanger sequencing in most diagnostic labs. Did the authors sequence non-coding exon 1 as well, please clarify.
7. Severity rating of the mutations section - lines 216-218 - it is very important to clearly state that what protein band of GAA protein as seen on Western blot is associated with each class of severity rating; i.e what protein bands were visible or missing in Class A, B, C categorized patients - precursor bands or mature band etc. Just saying protein band present does not suffice for this rating analysis.

8. line 236 - Excluding the outliner - should be outlier not outliner. Likewise line 251 - it should conversation with the referring physician, not conversation of the referring physician; line 259 - should be myopathies facies not myopathies facie.

9. Line 275 - c.1327-2A>G is IVS8 intronic splicing mutation and not an in frame deletion as depicted by authors - please check and correct and clear about it.

10. line 276 - p.Asn675del - is an in frame deletion, please check and correct it.

11. Line 280 - variants c. 1726 G>A and c. 2065G>A - are both well-known and well documented pseudodeficiency alleles and they should be written as such. Should not be written as GAA mutations.

12. Line 304 - Protein band at 76Kda is a well-documented and published mature GAA protein band along with 70Kda band. It should not be written as an intermediate band size. Most adults show both these band sizes on western blots.

13. Line 307 - Have authors sequenced protein band at 36Kda to make sure that it is indeed GAA protein band. Good to do that to make sure that it is not a spurious band being picked up. There is no mention of this 36Kds band in literature for GAA protein.

14. Discussion - line 390 - again grammatical mistake, "should be educated to specialists" is wrong - please correct this sentence. Same thing with line 394-395 - correct the sentence in these lines. Does not make sense to read it.

15. Authors should mention in their discussion section - importance of new born screening for early diagnosis of IOPD and obtain full benefit from early treatment with ERT.

16. Authors should also emphasize the importance of maintaining local mutation database along with CRIM and protein status so that future patients and treating physicians can benefit from this information.

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.

Yes

Are the conclusions drawn adequately supported by the data shown?
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Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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Not relevant to this manuscript

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Needs some language corrections before being published

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