Reviewer’s report

Title: Mortality in children with classic congenital adrenal hyperplasia and 21-hydroxylase deficiency (CAH) in Germany.

Version: 1 Date: 23 Mar 2018

Reviewer: Maria Vogiatzi

Reviewer's report:

I have the following questions and comments for the authors:

1. Results: The authors state that "Of the 14 CAH patients who died, 11 patients had the SW form of the disease and three females were classified with the SV form". Later on, at the same paragraph, they report "Molecular genetic classification of the severity of CAH was only possible in 8 cases, because 6 children with SV-CAH were not analyzed". How do the authors explain the discrepancy in the number of children affected with SV-CAH?

2. Results- 1st paragraph. Please explain what "0 genotype" and "A genotype" means.

3. Discussion, page 7, last line: What is the "uncomplicated" form of CAH? Do the authors use this term to describe the non-classical or mild form of 21OHD? Did the authors requested mortality data for non-classical 21OHD in their surveys?

4. Discussion, page 9, 2nd paragraph. The authors report "diarrhea" as one of the well-known SYMPTOMS of adrenal crisis. I am not aware of this. Can they provide a reference?

5. Discussion, page 9, 2nd paragraph, last line. Please provide a reference for the secretion of anti-diuretic hormone in adrenal crisis.

6. The authors used the AQUARE database to calculate mortality rates in CAH in Germany. When the database was established? Does it include classical and non-classical 21OHD or other types of CAH? The database collects information from 26 centers in Germany, and therefore, some CAH cases may have not been included. The authors need to describe their methodology for calculation of mortality rate and include their findings in the RESULTS section. At the moment, the mortality rate results appear only at Discussion, page 9, last paragraph.

7. Abstract- conclusions: The authors state that "All deaths could be related to an inadequate administration of stress doses.". However, they do not provide any related data in their
Abstract- Result section, so their conclusions appear unsupported under the current abstract format.

Minor comments

1. Abstract, 1st line: Consider changing to "Adrenal crisis in children with classic congenital adrenal hyperplasia…" as adrenal crisis can be life-threatening in both SW and SV forms.

2. Page 4: The authors state that the data were collected "pseudonymously". Do they mean "anonymously"?

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?
If not, please explain in your comments to the authors.

Yes

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If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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