Reviewer’s report

Title: Exon sequencing of the alpha-2-globin gene for the differential diagnosis of central cyanosis in newborns: a case report

Version: 1 Date: 03 Apr 2019

Reviewer: Nasir Al-Allawi

Reviewer's report:

The manuscript titled " Exon Sequencing of alpha 2 hemoglobin gene for the differential diagnosis of central cyanosis in newborns: A case report" reports on an interesting case of inherited methemoglobinemia due to a mutation in the alpha 2 globin gene leading to hemoglobin M. Such a de novo mutation is rare and especially as alpha variants of Hb M (Boston in this report) are rarer than the beta ones. The authors also stress the importance of keeping this diagnosis in mind when facing a case of a newborn with cyanosis, and they emphasize on some important clues, though well described previously, to such a diagnosis which include low SO2 by pulse oximetry but a normal PaO2.

There are few issues that may be worth considering:

1. Abstract : in the conclusions page 2 line 51-52. The statement need to be modified. And it could be said that methemoglobinemia maybe fatal in severe case, not generally fatal as in the statement.

2. Background page 3 lines 9-12, the statement should be clarified. It could be mentioned that Hb M is one of the causes of inherited Methemoglobinemia. Or they could mention the enzyme deficiencies as well as Hb M are cause of inherited Methemoglobinemia.

3. Page 4 lines 9-12, What method was used to determine the Hb variants, was it HPLC, cellulose acetate, or capillary electrophoresis?

4. Page 4 lines 14-19, Actually to my knowledge HBA2 c.175C>T which leads to Hb M Boston involves Amino Acid 58 as per references cited by the authors. Could the authors double check this and correct if necessary.

I think the manuscript is interesting and worth publishing provided the minor issues above are addressed.
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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