Reviewer’s report

Title: Fibrinogen Caracas IX. A novel fibrinogen mutation: FGA g. 3057 C>T (p. Arg104>Cys) impair fibrinogen secretion

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Reviewer: Johnny Mahlangu

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Fibrinogen Caracas IX. A novel fibrinogen mutation: FGA g. 3057 C>T (p.Arg104>Cys) impaired fibrinogen secretion

In this manuscript, the authors describe a novel fibrinogen mutation in an 11 year proband and her father. Structurally, Fibrinogen Caracas is a result of novel heterozygous g. 3057 C>T mutation in the FGA that predicts a p. Arg104>Cys substitution, in the proband and her father. Functionally this mutation interferes with the plasmin binding site with resultant impaired secretion. Both the proband and her father were clinically asymptomatic with low function and antigen levels.

In this manuscript, the authors have performed a number studies to characterize the protein. These include polymerization which was normal, plasmin degradation test which was normal, immunoblotting which was normal, clot structure analysis by confocal microscopy which was also normal.

The following queries require the authors attentions:

1. Since hypodysfibrinogenaemia could result in thrombosis, in this girl and father who were asymptomatic, how was thrombosis excluded

2. For this autosomal dominant condition, how can the discrepancy of the proband of 12% turbidity and that of the father of 40% turbidity be explained

3. It would of interest to indicate what the outcome of the nasal surgery was in the proband

4. In figure 1, the y-axis should be labelled

5. The manuscript should be shortened

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

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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