Reviewer’s report

Title: Factor V Leiden G1691A and Prothrombin G20210A mutations among Palestinian patients with sickle cell disease

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Reviewer: Chatree Chai-Adisaksopha

Reviewer's report:

Samarah et al. conducted a study investigating the prevalence of FVL and prothrombin gene mutation in patients with sickle cell disease. The findings were interesting. However, the conclusion of this study might be misleading.

Major comments

1. Authors did not describe well regarding the study design. I assumed that the study was conducted as a cross-sectional study.

2. Participants selection was not well described. Did you include consecutive patients with SCD registered in a single center? Did you have inclusion and exclusion criteria? Please describe.

3. The control participants were not well described. How did you recruit participants? Did you have inclusion and exclusion criteria? Did you perform matched-pair with the study cohort?

4. I wondered if sickle cell and thalassemia laboratory was carried out in both SCD patients and control populations or not. Please provide more detail.

5. It is not clear to me what data were collected at baseline. Authors stated that "None of the subjects experienced any past or current thrombotic events or had a family history of venous or arterial thrombosis…". Was that the exclusion criteria? If not, baseline characteristics should be in the results.

6. Table 1 should provide more detail about participants' demographic data; age, sex, history of arterial and venous thromboembolism and other co-morbid diseases. There was no data about control populations in the table.
7. Methods; page 4, please indicate whether it was mean age with standard deviation or others.

8. Authors did not report race of the participants. Since race is strongly associated with inherited thrombophilias, I would be interested to know the race of participants.

9. Page 6, authors described about the stroke, venous thrombosis and chronic leg ulcers. There was not mentioned anywhere in the methods. How did authors collect these data? Please describe whether authors reviewed medical records or patients reported their history by themselves. Did all vascular events occurred prior patients were enrolled or after?

10. Table 2 was not displayed properly. Authors wanted to compare the vascular events among patients with SCD and control. I suggest that authors should drop table 2 and add thromboembolic events in Table 1 (if the data were collected at baseline).

11. Page 7, line 18-22, odds ratio comparing between SS patients and control populations? Please provide more detail.

12. I did not fully understand why authors performed the logistic regression analysis, adjusting with age and sex. Please explain the rationale.

13. Did authors performed analysis comparing the association between all thromboembolic events and the presence of FVL?

14. Authors reported association between prothrombin gene mutation and stroke. This analysis was not mentioned in the methods.

15. Authors reported clinical symptoms of SCD but there was not mentioned in methods.

16. Authors concluded that FVL was more prevalent among SS patients compared to control. There were a lot of unclear information regarding participants' race, and participant selection. In addition, sample size of this study was small and authors found the difference in SS subgroup only. I would suggest authors to take this sentence away. Can authors provide more biologic rationale why SS patients would be more prevalent to have FVL?
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

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.

No

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.

I am able to assess the statistics

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