Reviewer’s report

Title: Chronic complications and quality of life of patients living with sickle cell disease and receiving care in three hospitals in Cameroon: a cross-sectional study

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Reviewer: Patrick Mcgann

Reviewer's report:

In this manuscript, the authors attempt to describe the clinical features and quality of life scores for a small cohort of patients with sickle cell disease at three centers in Cameroon. The topic is an important one as some patients in low and middle income countries do survive childhood, and few studies have described the long term sequelae of living with sickle cell disease in this setting. Quality of life receives little attention for people living in sub-Saharan Africa in general, and more data on this aspect of health is welcomed. While the clinical question, particularly in a cohort of patients in Africa, is of merit, the manuscript and message could be considerably improved if the authors address the following comments.

Major Comments:

1. Abstract: The authors’ aims are stated in the abstract, but the introduction does not provide a focused background to chronic complications of sickle cell disease or quality of life. The description of Methods is vague and it is not clear how the participants were selected from these 3 centers or how the questionnaires were assessed. The SF-36 should be introduced to the reader in the Methods section of the Abstract for those not familiar with what this test is. The results should begin with the number of patients and basic demographics. In the Conclusions, the authors state that care is sub-optimal, though the study does not appear to attempt to evaluate or report the delivery or quality of clinical care. Overall, the use of English language and grammar could be improved. Additional comments below from the main text should be cross-checked upon revision of the abstract.

2. As a whole, the Background text could benefit from improved citation of biomedical literature rather than third party summaries of the medical literature. For instance, the fact that SCD is often associated with chronic complications could be supported with reference to either an excellent review article about the chronic complications of sickle cell disease as a whole (for example Thein MS et al. Sickle cell disease in the older adult. Pathology. 2016 Nov 30, or Ballas SK et al. Beyond the definitions of the phenotypic complications of sickle cell disease: an update on management. Scientific World Journal. 2012;2012:949535) or individual references regarding specific chronic complications.
3. Background, line 56, the authors state that the WHO has "placed SCD in the 4th position of public health priorities" with citation #3 identified as the source. I am not familiar with the WHO ranking public health priorities or that SCD is among the top 5 priorities. If so, this should be more clearly stated and appropriately referenced.

4. The authors should include comment on the existing literature regarding QoL in SCD, as this is a large part of this study. A brief introduction with appropriate references to what we know about QoL in SCD (outside of Cameroon) would help to set the stage for the rest of the text.

5. In the Methods section, the authors identify three institutions in Cameroon and Figure 1 identifies 182 "eligible patients" but it is not clear what defines eligibility. Anyone presenting to the center on a particular day? Are there only 182 patients cared for between these 3 institutions? It would be helpful to describe the size and capacity of the sickle cell center at each of the three settings. Additionally, it would be helpful to understand these centers in respect to geography, economy, population, and health care resources. I see on a map that these centers are opposite corners of the country. Does this change the patient population?

6. The authors describe a "cross sectional study" over 5 months. More details about how the study was actually performed is required. How were the patients identified and approached? Was this in a sickle cell clinic? A general clinic? An inpatient setting? Or more than one setting? How many patients were recruited from each hospital/center?

7. The authors refer to their sample size calculation with a reference from a manuscript from Jamaica. Did they just assume the sample size and study design were the same? A more statistically appropriate description of sample size and power would be helpful. A sample size of 110 is necessary to detect what type of difference in QoL between these groups of patients? The study only has 9 patients from a rural area. Does the sample size require equal numbers in each group? Was sample size calculated before the study was performed? If this is merely a convenience sample that was obtained during a specific time frame, this should be stated without trying to identify a sample size that is not relevant for this particular study.

8. The data collection tools are a critical aspect of this manuscript and are not well described. How was the data regarding history of chronic complications elicited from patients/guardians? What questions were asked? What definitions were used for "heart disease" or "avascular necrosis of the hip"? How many different investigators performed these questionnaires? Were these asked of the patients or was the medical record used? Do these centers have comprehensive medical records with such data?

9. The description of the patients would be improved with evaluation of additional, more common sickle cell complications, such as acute chest syndrome or respiratory disease? Why don't they ask questions about number of hospitalizations or number of How was the
list of complications selected? The data collection tool should be added as supplementary material.

10. Methods, line 76 states that only children above 5 were included. Were specific ages used as inclusion/exclusion criteria? Stroke can certainly occur before age 5. The comment that stroke can happen "as early as age 5" should be reworded. The authors should clearly state the inclusion/exclusion criteria for these patients and why patients less than age 5 were excluded.

11. More information about the SF-36 should be included either here or above. What is the total score? What is a good score or bad score? From my reading, it appears a score of 50 is normal, above 50 is better than normal and less than 50 is less than normal? Based on the data, it appears this cohort has a good quality of life? Has this tool been translated into French and/or local languages? In which language was it administered? Has it been validated in that population? If translated, has the translation been confirmed to be correct?

12. What type of gel electrophoresis was used? HPLC? Are quantities of HbS, HbF, and HbA2 known? If so, this data would be helpful.

13. Are there laboratory data available for these patients? A table summarizing available laboratory data, particularly hematology data (Hb, MCV, HbF, etc), would improve the quality of this manuscript.

14. Results, line 110. What does it mean that vaccinations are or are not up to date. If full vaccine data is available, this should be presented in its entirety. For example, what percentage of patients have received pneumococcal vaccination, Haemophilus influenzae, type B, polio, Hepatitis B, etc. The comment that 59% of patients do not have vaccines "up to date" is not meaningful on its own.

15. How were the chronic complications defined? The text (lines 116-120) select random data points that are not of great interest and difficult to follow. The authors should more clearly summarize the important findings in this section.

16. Why is a systolic murmur mentioned (line 120)? Was this identified by physical exam? Or by report from parents? It is not clear if these data were collected by extracting medical records, by asking the patients, by examining the patients or a combination of these methods. This should be more clearly defined.

17. The QoL data (page 6, line 122-135) needs to be more clearly summarized. How many total sections were there and how is the score calculated? Is the total score just the physical component score plus the mental component score?

18. When it says that "holding every else constant" it is not clear what variables are included in the multivariable model. Variables not present in the tables have been mentioned in the
results section. Please be more explicit about what variables have been included in your multivariable model.

19. Overall, with significant revision, the Discussion should be restructured to highlight the important findings of this study and succinctly pass along the primary message of the research to the reader. In its current form, the Discussion is too verbose with too many stated comparisons to literature that is not entirely relevant to the current work.

Figures/Tables

1. Figure 1 mentions 2 participants that died during the course of the study. I believe this study was a cross sectional analysis with data collected at a single time point. How was this possible for a patient to die during the study?

2. Table 3 is not helpful. Summarize this data in the text, particularly the number of patients taking hydroxyurea. What are the "vasodilators" and what was the indication for their use?

3. Figure 4 - does not add much value to the manuscript, but makes sense that agreement between the total score and the individual scores would be better than the agreement between the mental and the physical.

Typographical and Grammatical Mistakes

1. In the abstract, the 2nd sentence of the background does not make sense. There is an extra verb. Possible rewording could be: "Most developed countries have reduced applied these recommendations with success, whereas their implementation in sub-Saharan African countries has been hindered by lack of information about the burden of the disease."

2. In the final sentence of the conclusions, the word new-born should not be hyphenated. This is typically a single word written "newborn."

3. Line 74, there is a superfluous "a" in the sentence that reads, "which has a the main sickle cell center…"

4. On line 128, the second sentence says "Holding every else constant…” and it should read "Holding everything else constant…”

5. The second sentence of the discussion is improper English and ought to be improved. It seems like the author means to communicate that chronic complications are common even though the population is young (median age 16 yo).
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.

No

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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