



SDI Review Form 1.6

PART 1:

Journal Name:	International Journal of TROPICAL DISEASE & Health
Manuscript Number:	2013_IJTDH_3838
Title of the Manuscript:	Pattern and risk factors for musculoskeletal complications of sickle cell anaemia in South-east Nigeria: a retrospective study

General guideline for Peer Review process is available in this link:

(<http://www.sciencedomain.org/page.php?id=sdi-general-editorial-policy#Peer-Review-Guideline>)

- This form has total 7 parts. Kindly note that you should use all the parts of this review form.



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PART 2: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
Compulsory REVISION comments	1. The last sentence of the abstract is unlikely to help patients or change outcomes based upon available data. Suggest removing this statement or revising (see general comments below). 2. Intro: Lengthy discussion on prevalence of SCA in Africa. Clarify the relevance to this paper. Suggest referencing Weatherall and Clegg, Bull WHO 2001. β^s prevalence in this ref. in Nigeria ranges 6-24%. rs334 in Yoruba hapmap is 21%, again emphasizing that the 24% allele frequency in all of Nigeria is likely an overestimate. 3. Intro: Please cite a reference for the increased mortality of musculoskeletal complications – I am not sure this is an accurate statement for so many complications combined into a single category. 4. Intro: Are leg ulcers in SCD known to be caused by venous stasis and tissue hypoxia? 5. Methods: Did subjects provide consent or was the study approved by the ethics committee allowing for collection of existing data? 6. Methods: Define specific criteria for all complications in Table 1 (especially musculoskeletal).	Thank you for the thoughtful comments. 1. The last sentence of the abstract has been revised as suggested. 2. The discussion on the prevalence of SCA in Africa has been shortened. The 6-24% prevalence reported by Weatherall and Clegg has been cited. 3. The statement increased mortality due to musculoskeletal complications has been deleted. 4. It has been postulated that these factors can predispose to sickle cell leg ulcers. The sentence has been modified. 5. This was a retrospective study and approval was obtained from the hospital's ethical committee to use existing data. This was stated under



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	7. Strongly suggest authors remove musculoskeletal category from Table 1 - diverse group with multiple manifestations. Recommend the same for Table 2 - this allows readers to focus on the 3 most common MS complication of SCD – ulcers, AVN and osteomyelitis. The age association for MSS is too confusing given that this is such a heterogeneous clinical group, and we know that some complications like ulcers increase with age. 8. For brevity, suggest using median or mean, but not both in Table 2. 9. Why does Table 2 have an abbreviation for VOC? 10. In discussion, perhaps the higher prevalence of osteomyelitis in developing nations is due to this being a more common diagnosis in everyone. The comparison group needed here are controls without SCA. 11. The Jamaican group has several publications on skin ulceration. Suggest citing these papers, as Jamaica is in many way the equivalent of some developing nations. Again, controls without SCA would be enlightening – one explanation is that ulceration just occurs more frequently in tropical climates (both tropical ulcers and SCD ulcers).	ethical approval just before the “result” section. 6. The specific criteria for all complications have been defined under the sub-heading diagnostic method. 7. Musculoskeletal category has been removed from Tables-1 and 2. 8. We have removed the mean in Table 2. 9. The abbreviation was included for brevity and spelt out fully as a foot note. 10. We agree with this comment and it has been reflected in our discussion. 11. We have included some publications from the Jamaican group.
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<u>Minor</u> REVISION comments	1. Intro: “due to a point mutation in the β globin gene”, not a point mutation in β^S. 2. There is an association between leg ulceration and elevation of tricuspid regurgitation, but this is not the same as pulmonary hypertension. In fact, PH associated with hemoglobinopathies will be removed from the WHO classification of PAH this year as a consequence of equating elevated TRV with PAH. See Bunn et al. Blood 2010.	1. This has been corrected. 2. The sentence has been re-written to reflect this illuminating comment.
<u>Optional/General</u> comments	Nice overview of SCA complications in Nigeria, although the study is significantly underpowered. However, the authors have again shown that AVN is associated with higher baseline haemoglobin in SCA. This implies association, and not causation, and therefore the conclusion that constant monitoring of the haemoglobin should be recommended in evaluating MSS complications is not warranted.	The conclusion has been re-written.