Reviewer's report

**Title:** Chronic Kidney Disease is common in Sickle Cell Disease: a cross-sectional study in the Tema Metropolis, Ghana

**Version:** 2  **Date:** 13 January 2015

**Reviewer:** Santosh L Saraf

**Reviewer's report:**

Major Compulsory Revisions:

1. **Methods:** Anthropometry: The weight status should be accurately defined in children. Using the adult BMI classifications for children is incorrect. Underweight should be based on < 5th percentile for age/gender, overweight 90 - 95th percentile for age/gender, obese > 95th percentile for age/gender.

2. **Results:** There are several things that need consideration:

   Hb SC patients were significantly older and age is a risk factor for CKD. Is it possible that age is confounding the difference in CKD stage 2 observed in Hb SC vs. Hb SS? Consider adjusting for age when comparing the 2 cohorts as a separate analysis or looking at prevalence of CKD in children vs. adults. This should at least be mentioned in the limitation paragraph.

   Relative hypertension is a risk factor for kidney disease and mortality in sickle cell disease. The prevalence of relative hypertension should be compared between genotype and by CKD status.

   Hyperfiltration may also be a risk factor for kidney disease in sickle cell disease. The prevalence of hyperfiltration should be compared between genotype.

5. **Results:** In the 3rd paragraph, a comparison is made between Hb SS and Hb SC with CKD. To understand the pathophysiology of CKD and see if pathways differ between genotype, it would be interesting to perform an additional analysis comparing those patients with vs. without CKD in each genotype (e.g. in Hb SS patients: CKD vs. No CKD, in Hb SC: CKD vs. No CKD).

6. **Discussion:** 2nd paragraph, 1st sentence, the prevalence of CKD is not higher in your cohort because you have combined pediatric and adult patients. Reference 1 is a pediatric cohort. Reference 19, which is an adult cohort, has a much higher prevalence of CKD than your cohort. If you want to compare prevalence between studies, would recommend looking at CKD prevalence in the pediatric cohort and adult cohort, separately.

7. **Discussion:** 3rd paragraph, 5th sentence, what evidence have you discussed to say anemia could cause glomerular damage? This sentence should be removed or have major changes. This is not a prospective cohort and perhaps the anemia is a consequence of the kidney disease (decreased Epo production) or both the CKD and anemia share a common pathophysiology (e.g. more severe hemolysis).
8. No Limitations paragraph: There are clearly limitations to this study as with any cross sectional study that should be noted. A single urine measurement was used to assess CKD – this can vary and the most accurate way to define CKD is with 2 consecutive urine measurements (this can be difficult but should be noted as a limitation). Urine albumin and protein concentrations can vary by time of collection (this needs to be clarified if this was a random vs. first vs. second morning urine specimen). If you are not doing age adjustment or looking at CKD by age category, this is a major limitation that needs to be mentioned.

Minor Revisions:
1. Abstract: In the second sentence of the Results section, should it state eGFR >/ 90 or should be < 90? More than 8.6% of Hb SS patients should have eGFR > 90 based on your tables.
2. Background: References do not appear to be correct. Please double check and correct them.
3. Methods: Blood pressure measurement – please clarify if this was performed manually or with an automated machine.
4. Results: Second paragraph, second sentence (see comment 1 in this section) – should it state eGFR >/ 90 or should be < 90?
5. Results: Third paragraph, last sentence is confusing. Please rephrase this sentence to make clarify your message.

Discretionary Revisions:
1. Background: 2nd paragraph, second sentence – recommend clarifying how renal disease was defined in these other cohorts.

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I have no competing interests to disclose.