Reviewer's report

Title: Determinants of Academic Performance in Children with Sickle Cell Anaemia

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Reviewer: Daniel Armstrong

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This manuscript reports on the relationship between school absenteeism, academic achievement, and intellectual function of 90 children with sickle cell anemia (SCA) and 90 age-similar classmate controls. The authors report significantly higher school absence in children with SCA, but no significant association between school absence and academic achievement, but did find a significant association between academic performance and both intellectual function and socioeconomic status.

The authors address an important question in a region where SCA is a major health problem with high impact on many features of life, including school achievement. The study was designed with close attention to recommendations from other investigators in this area, and the findings are both important and relevant.

There are a few issues the authors and editors may want to consider.

Major Compulsory Revisions

1. The supporting literature is not up-to-date. Many of the cited references are from the late 1980s and early 1990s, and one of the foundational references (Chordokoff and Whitten, 1963) has subsequently been challenged by multiple studies that have shown significant neurocognitive deficits in children who experience stroke, silent cerebral infarct, and even those with no neuroimaging abnormalities who demonstrate as much as a 1 SD decline in function over the school-age years of life (Wang et al, 2001). Recent papers have also reported decreased function in children with indeterminate Transcranial Doppler (TCD) flow rates (e.g, Boni et al), and a strong association between poor neurocognitive function and low hemoglobin in neurologically intact adults with SCA (Vichinsky et al, JAMA, 2010). The failure to address these more current reports detracts from the interpretation of the results of the study.

2. The use of the DAPT as the primary measure of intellectual function is a limitation, since this test does not assess verbal function and relies on functions that have been documented as being at risk in children with SCA (e.g., visual-motor coordination, processing speed). Because of this narrow focus, the DAPT may over or under-estimate cognitive function in individual children. This issue should be addressed by the authors.
3. One of the major differences between this study and some of the published studies on academic achievement is that the published studies used a standardized measure of academic achievement while this study used averages of more subjective grades. These grades are dependent on the grading practices of the individual teachers, and cross-teacher reliability was not assessed. The authors should provide a rationale for this measurement strategy and provide some discussion of this limitation.

Discretionary Revisions

4. One of the major differences in this cohort and the other published studies is the high rate of malaria, something that is rare to non-existent in the US, UK, or other countries. This could be a significant unique factor in school absenteeism and should be emphasized as a difference in the paper.

5. Pain resulting in hospitalization is but one mechanism for school absenteeism. Eaton et al found that children who were not hospitalized for pain still experienced a significantly higher number of school absences than healthy controls. It would be helpful to know how much daily pain not requiring hospitalization was associated with absence.

6. The finding that academic scores declined between 6 to 9 years and flattened thereafter is consistent with the finding of Wang et al (J Pediatrics, 2001) of decline in intellectual function over time in children with no abnormal neuroimaging evidence.

7. The section on use of blood transfusion is confounded, since the need for transfusion could affect absence, intellectual function, and achievement, but receiving chronic transfusion may improve function. Some additional attention to this relationship should be included in the paper.

This is an important and relevant paper, but the context of the study needs to be improved by including a review of more current research findings in this area.

Level of interest: An article whose findings are important to those with closely related research interests

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

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I have no competing conflicts of interests to declare related to this manuscript.