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*Editorial Comment*

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# Renal involvement in sickle cell disease: an African perspective for an African condition

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Homozygous sickle cell disease (HSCD) is a life-threatening and debilitating condition, with high mortality rates recorded even in affluent countries such as the USA, where the median survival of HSCD patients is 40–50 years [1]. In recent decades, a myriad of interventions such as a chronic transfusion programme, vaccination, antibiotic prophylaxis and early recognition of crises have played a key role in achieving these improved survival figures. Such interventions, often very costly, are mostly confined to richer nations with sophisticated healthcare systems. In Equatorial Africa, the bedrock of sickle cell disease in the world (Figure 1), the median survival is still very low. Accurate data are lacking but the majority of children born with HSCD in Sub-Saharan Africa are probably unlikely to see the end of the first decade of life [2]. Such abysmal mortality figures, completely in discord with improvements seen elsewhere, need to be brought to the public domain, backed by data from local studies in areas where the disease is endemic. Such studies will not only provide accurate data regarding the urgency to tackle this issue, but also guide locally relevant and adapted disease combat strategies, and may uncover local disease idiosyncrasies which may render 'imported' strategies relatively ineffective [3]. For instance, a well-conducted, bacteriological study in Uganda found *Staphylococcus aureus* (60%) to be the leading cause of bacterial infections in febrile children with sickle cell disease, not *Streptococcus pneumoniae* (19%), raising questions about the justification of routine pneumococcal vaccination in African sufferers [4].

In a large cohort followed up by Platt *et al*. [1], renal failure was the predominant organ failure, found in 40% of HSCD patients who died (7.6% of the overall study population). This suggests that interventions to identify, prevent and promptly treat renal involvement in HSCD will save many lives and help improve the dismal mortality figures seen with this condition. Renal abnormalities in HSCD have been previously well characterized, the *primum movens* being microvascular obstruction causing an ischaemic glomerular and/or tubular injury resulting in cortical infarction, papillary necrosis, focal segmental glomerulosclerosis, tubular atrophy and interstitial fibrosis in the main [5]. The main clinical syndromes associated with these include proteinuria (in approximately 20–30% of cases), haematuria, glomerular hyperfiltration, impaired concentration ability, renal tubular acidosis and chronic renal insufficiency [5]. Proteinuria, haematuria and severe anaemia have been shown to be the independent predictors of progression to chronic renal insufficiency [6]. As such, interventions to address these, such as the use of hydroxyurea, a proactive transfusion programme, and the routine use of ace inhibitors and angiotensin receptor blockers, are now standard practice in HSCD patients [7]. Such evidence-based interventions, however, do not seem to have achieved universal adoption, particularly in high prevalence areas such as Sub-Saharan African countries; if they have, the extent is unclear due to the paucity of studies.

In this issue of *CKJ*, Kaze *et al*. [8] report the renal abnormalities found in a reasonably large cohort of Cameroonian children and adults homozygous for sickle cell disease. Various American and Caribbean studies have previously reported the predominant renal clinical findings in sickle cell disease to be albuminuria, proteinuria, glomerular hyperfiltration and reduced glomerular filtration rate (GFR), with the majority of such studies looking at a paediatric population [7, 9–11]. In Yaoundé, Cameroon, an equatorial city where sickle cell disease is endemic, Kaze *et al*. recruited 72 treatment (ACE-I and hydroxyurea) naive HSCD adults and children and measured their renal function, blood pressure, urine protein, albumin and levels of red and white blood cells in the urine. It was staggering to find a 9 in 10 prevalence of overt proteinuria (protein–creatinine ratio >200 mg/g) in this cohort [8]. This indicates that almost all of these patients had some degree of renal damage requiring urgent intervention to prevent further nephron loss. Recently, Bolarinwa *et al*. reported a much lower prevalence of proteinuria (microalbuminuria and albuminuria) in a somewhat similar population from Western Nigeria [12]. This Cameroonian cohort clearly presents a much higher frequency of proteinuria than seen in other parts of the world. It will seem from this data that proactive routine ace inhibition is not yet the rule in the setting of this study, but whether this fully explains the finding remains to be seen. We look forward to data following therapeutic interventions, from the authors and other research groups in similar settings. Disease duration was found to be a key factor associated with proteinuria, as mean and median protein–creatinine ratios increased with increasing age quartile, and hence increasing the disease duration.

Almost all of the patients had serum creatinine values within the normal range, translating into 'normal' GFRs

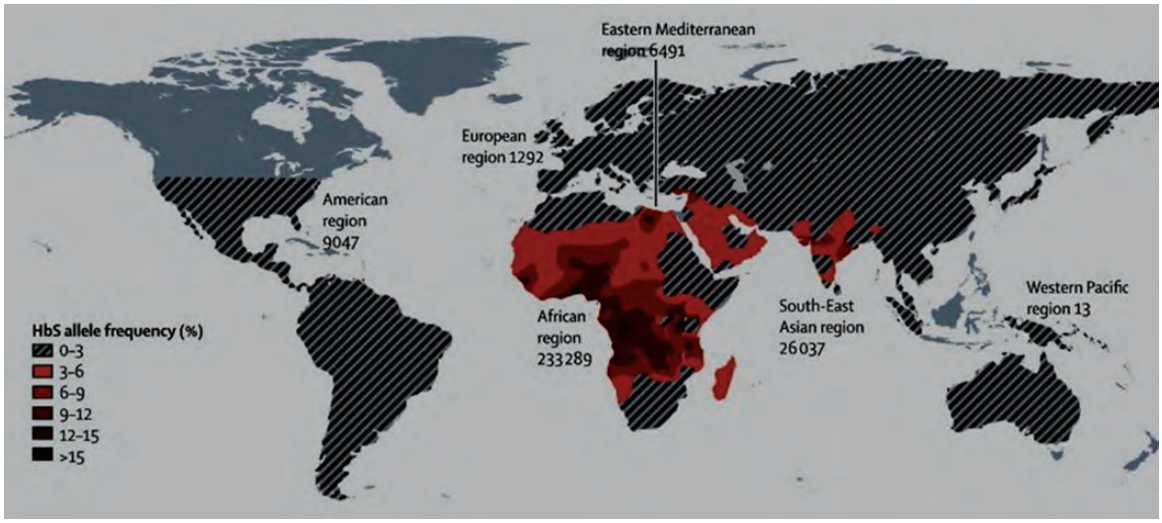


**Fig. 1.** Distribution of the prevalence of the sickle cell allele in the world. The highest frequency of the sickle cell allele is found in Sub-Saharan Africa, particularly in areas around the equator, where the prevalence often exceeds 15% (dark brown). Yaoundé, the capital city of Cameroon, where this study took place is found in this highest frequency belt. The numbers represent the estimates of the total number of people afflicted by HbSS, HbSC and HbSß-thalassemia per World Health Organisation region [13]. Figure adapted and reprinted from David Rees, Thomas Williams and Mark Gladwin, Sickle-cell disease, *Lancet* 2010; 376: 2018–2031 (Copyright 2010), with permission from Elsevier.

estimated by any of the currently used formulae. However, a 30.5% prevalence of glomerular hyperfiltration, also seen by other investigators [12], indicates that these so-called normal GFRs may be falsely reassuring, as hyperfiltration will have undoubtedly resulted in a lower serum creatinine than will reflect the 'actual' kidney function, if it were possible to measure this by a more accurate means. The estimated kidney function, even when adjusted for body weight with the Cockcroft–Gault formula, reduced with increasing disease duration ($P = 0.04$). Interestingly, none of the patients in this cohort had a raised blood pressure, although an association was found between systolic blood pressure and lower eGFR ($r = 0.4$, $P = 0.003$).

In all, this study informs us of a particularly high prevalence of overt proteinuria in African HSCD patients who were not receiving the classical interventions of ACE-I and/or hydroxyurea, both relatively affordable and safe interventions that have been clearly shown to halt or reverse progression of renal disease in these patients. One would have wished to perhaps see a larger cohort, a control group, ultrasonographic and histological data, some longitudinal data following intervention, the influence of local factors such as malaria, but this still remains a laudable effort by Kaze *et al*., providing some baseline data to inform such future studies and guide clinical management. Such studies in the areas of high disease prevalence but where clinical research can be very challenging due to resource limitations and the high demands of clinicians' workloads should be encouraged and supported as they are likely to provide area-specific data that would not necessarily have been transferable from studies in richer western countries as is often the case.

*Conflict of interest statement.* None declared.

(See related article by Kaze *et al*. Kidney function, urinalysis abnormalities and correlates in equatorial Africans with sickle cell disease. *Clin Kidney J* 2013; 6: 15–20)

## References


1. Platt OS, Brambilla DJ, Rosse WF *et al*. Mortality in sickle cell disease—life expectancy and risk factors for early death. *N Engl J Med* 1994; 330: 1639–1644
2. Diallo D, Tchernia G. Sickle cell disease in Africa. *Curr Opin Hematol* 2002; 9: 111–116
3. Serjeant GR. Mortality from sickle cell disease in Africa. *BMJ* 2005; 330: 432–433
4. Kizito ME, Mworozi E, Ndugwa C *et al*. Bacteraemia in homozygous sickle cell disease in Africa: is pneumococcal prophylaxis justified? *Arch Dis Child* 2007; 92: 21–23
5. Pham P-TT, Pham P-CT, Wilkinson AH *et al*. Renal abnormalities in sickle cell disease. *Kidney Int* 2000; 57: 1–8
6. Powars DR, Elliott-Mills DD, Chan L *et al*. Chronic renal failure in sickle cell disease: risk factors, clinical course, and mortality. *Ann Intern Med* 1991; 115: 614–620
7. Stallworth JR, Tripathi A, Jerrell JM. Prevalence, treatment, and outcomes of renal conditions in pediatric sickle cell disease. *South Med J* 2011; 104: 752–756
8. Kaze FF, Kengne A-P, Atanga LC *et al*. Kidney function, urinalysis abnormalities and correlates in equatorial Africans with sickle cell disease. *Clin Kidney J* 2013; 6: 15–20
9. Dharnidharka VR, Dabbagh S, Atiyeh B *et al*. Prevalence of microalbuminuria in children with sickle cell disease. *Pediatr Nephrol* 1998; 12: 475–478
10. Wigfall DR, Ware RE, Burchinal MR *et al*. Prevalence and clinical correlates of glomerulopathy in children with sickle cell disease. *J Pediatr* 2000; 136: 749–753
11. King L, MooSang M, Miller M *et al*. Prevalence and predictors of microalbuminuria in Jamaican children with sickle cell disease. *Arch Dis Child* 2011; 96: 1135–1139
12. Bolarinwa RA, Akinlade KS, Kuti MA *et al*. Renal disease in adult Nigerians with sickle cell anemia: a report of prevalence, clinical features and risk factors. *Saudi J Kidney Dis Transpl* 2012; 23: 171–175
13. Modell B, Darlinson M. Global epidemiology of haemoglobin disorders and derived service indicators. *Bull World Health Organ* 2008; 86: 480–487


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