

Sickle Cell Trait Associated With Increased Risk of Renal Disease

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Sickle cell disease is a hereditary blood disorder characterized by abnormal red blood cells that are prone to adopting a rigid, sickle-like shape. An autosomal recessive condition, individuals with two copies of the sickle hemoglobin mutation have sickle cell disease, while individuals inheriting only one copy have sickle cell trait, which is generally considered benign. While renal disease in the context of sickle cell disease is well established, the relationship between sickle cell trait and renal disease is less known. In a recent report in the *Journal of the American Medical Association*, Dr. Alex Reiner in the Public Health Sciences Division led an effort to characterize the potential association between sickle cell trait and chronic kidney disease. The results from this study suggest that sickle cell trait may be associated with higher risk of kidney disease in African Americans.

The sickle cell mutation (rs334 in the *HBB* gene) is more common in individuals of African ancestry than other populations, and an estimated 1 in 12 African Americans are affected by sickle cell trait. African Americans also have a disproportionately higher risk of chronic kidney disease and progression to end-stage renal disease. While renal complications have been reported in those with sickle cell trait, the extent of this relationship is not known. According to senior author Dr. Reiner, "our findings suggest that sickle cell trait appears to be one factor that contributes to the higher burden of kidney disease among that population."

To characterize this relationship, the authors combined data from five large population-based, prospective cohort studies in the United States, totaling nearly 16,000 participants. This allowed the researchers to evaluate the associations between sickle cell trait and several kidney function outcomes: chronic kidney disease, incident chronic kidney disease during follow-up, estimated glomerular filtration rate (eGFR), end stage renal disease, and albuminuria. Compared to non-carriers, the authors found that sickle cell trait carriers had significantly increased risk of chronic kidney disease, decline in eGFR, and albuminuria (see figure).

Compared to non-carriers, those with sickle cell trait had a 57% increased risk of chronic kidney disease and an 86% increased risk of albuminuria. These associations appeared to be independent of *APOL1* risk variants, which have also been associated with chronic kidney disease progression in

African Americans. Several sensitivity analyses suggested these findings to be fairly robust. "There was remarkable consistency of the results across the 5 studies, even though they were composed of different ages and sex distributions," said Dr. Reiner.

Since sickle cell trait carriers are often identified at an early age, these findings could be potentially useful for developing early detection and intervention programs to improve outcomes. More research is needed, however, in order to ensure the appropriate translation of these findings. "There have been national pushes for screening of sickle cell trait in several different contexts (e.g., reproductive health; military or college athletics due to a possible increased risk of exercise-induced sudden death)," said Dr. Reiner, "but little guidance about what to do medically with such screening information. Moreover, the current results DO NOT indicate that every single person with sickle cell trait is going to develop kidney disease. While it is possible that sickle cell trait screening may ultimately be found to have utility for early detection of kidney dysfunction and whittling of health disparities faced by African Americans, further investigation will be necessary to yield specific recommendations."

Overall, these findings suggest that sickle cell trait contributes to the racial disparity in chronic kidney disease. "This study highlights the need for additional research into the health consequences of sickle cell trait," said Dr. Reiner. "Future studies might evaluate possible associations between SCT and other chronic vascular-related diseases such as retinopathy, stroke and other conditions."

[Naik RP, Derebail VK, Grams ME, Franceschini N, Auer PL, Peloso GM, Young BA, Lettre G, Peralta CA, Katz R, Hyacinth HI, Quarells RC, Grove ML, Bick AG, Fontanillas P, Rich SS, Smith JD, Boerwinkle E, Rosamond WD, Ito K, Lanzkron S, Coresh J, Correa A, Sarto GE, Key NS, Jacobs DR, Kathiresan S, Bibbins-Domingo K, Kshirsagar AV, Wilson JG, Reiner AP.](#) 2014.

Association of sickle cell trait with chronic kidney disease and albuminuria in African Americans. *JAMA*. 312(20):2115-25. doi: 10.1001/jama.2014.15063.

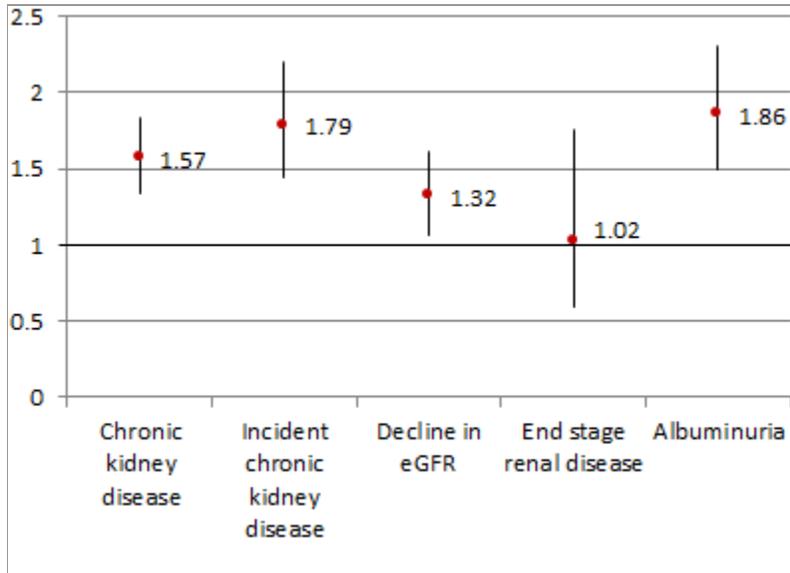


Image provided by Dr. Jonathan Kocarnik

Odds ratio estimates for the association between sickle cell trait and renal disease outcomes, compared with non-carriers (eGFR = estimated Glomerular Filtration Rate).