

Study identifies 'silent' stroke risk factors for children with sickle cell anemia

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Factors such as low hemoglobin levels, increased systolic blood pressure, and male gender are linked to a higher risk of silent cerebral infarcts (SCIs), or silent strokes, in children with sickle cell anemia (SCA), according to results from a large, first-of-its-kind study [published online](#) today in *Blood*, the Journal of the American Society of Hematology (ASH).

Silent strokes are the most common form of neurological injury found in SCA, with more than 25 percent of children with the disorder suffering a SCI by age six,¹ and nearly 40 percent by age 14.² Strokes occur in patients with SCA as a result of low hemoglobin levels in the blood. Because hemoglobin is responsible for carrying oxygen to the blood, the body compensates for low hemoglobin levels by increasing blood flow to the brain, raising patients' risk for [brain injury](#), including these [silent strokes](#).

"Young patients with a history of silent strokes have an increased risk of future overt strokes and new or increasingly severe silent stroke-related events, and have poorer cognitive function than children with sickle cell disease who have normal brain MRIs," said Michael R. DeBaun, MD, MPH, first author and initiator of the study and Director of the Vanderbilt-Meharry Center for Excellence in Sickle Cell Disease at Vanderbilt University. "Children with silent strokes have a much higher risk of [poor academic performance](#), and over the long term, we see a higher proportion of these young adults requiring special education or being retained in school."

While silent strokes have been well documented in [older adults](#), there has been limited research available to support clinical [risk factors](#) for silent strokes in children with SCA. In order to assess whether previously identified risk factors for silent strokes in the general population -- low hemoglobin, high [systolic blood pressure](#), and male gender -- were also associated with an increased risk of silent strokes in patients with SCA, investigators analyzed data from the international, multicenter Silent Cerebral Infarct Multi-Center Clinical Trial (SIT Trial). The SIT Trial, which was supported by the National Institutes of Health (NIH) and the National Institute of Neurological Disorders and Stroke (NINDS), was designed to determine the efficacy of blood transfusion therapy for prevention of recurrent silent stroke events in participants with SCA.

In this cross-sectional study, investigators evaluated clinical history and baseline laboratory values and performed brain MRIs (to confirm silent stroke) in 814 children with SCA between the ages of 5 and 15 years with no history of overt stroke or seizures. Results from the data analysis showed that silent strokes occurred in one-third (251 of 814) of SCA patients enrolled in the trial. Further analysis demonstrated that lower concentrations of hemoglobin, higher baseline systolic blood pressure, and male gender were associated with a significantly increased risk of silent stroke.

"This study confirms our original hypothesis that risk factors for silent strokes in the general population are also risk factors for pediatric patients with sickle cell anemia," said Dr. DeBaun, also the JC Peterson Endowed Chair in the Department of Pediatrics at Vanderbilt University. "With these results, we can focus our research efforts on strategies to prevent these silent strokes in children with SCA."

Dr. DeBaun and colleagues are currently conducting additional research to determine if hydroxyurea, a treatment traditionally used to manage the pain episodes that occur with SCA, can also be used to prevent silent

strokes in infants.

More information: Kwiatkowski JL, Zimmerman RA, Pollock AN, et al. Silent infarcts in young children with sickle cell disease. *Br J Haematol.* 2009;146:300-305.

Bernaudin F, Verlhac S, Arnaud C, et al. Impact of early transcranial Doppler screening and intensive therapy on cerebral vasculopathy outcome in a newborn sickle cell anemia cohort. *Blood.* 2011;117:1130-1140; quiz 1436.

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