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High blood pressure in the lungs a major risk for death in adults with sickle cell disease

Bethesda, Maryland — A new study reveals that nearly one third of adults with sickle cell disease develop high blood pressure in their lungs and that the condition, known as pulmonary hypertension, causes a much higher death rate in patients with the complication than those without it. The findings, according to researchers from the Warren Grant Magnuson Clinical Center at the National Institutes of Health (NIH), demonstrate an urgent need to diagnose this complication in adults with sickle cell disease as it is a major risk factor for death. The study was conducted as a multi-center collaboration between NIH and the Howard University Center for Sickle Cell Disease. A complete report will publish in the February 26 edition of the New England Journal of Medicine.

Sickle cell disease is a chronic, often fatal anemia that is classically characterized by severe attacks of pain from blood vessels being blocked by red blood cells that become rigid and form a sickle shape when deoxygenated. In the United States this genetic disease occurs predominantly in people of African descent, and is accompanied by episodic severe pain in the joints, leg ulcers, jaundice and multi-organ failure. A serious complication of sickle cell disease is pulmonary hypertension.

Pulmonary hypertension is high blood pressure (not related to the pressure measured by cuff on the arm) in the arteries that supply the lungs. The blood vessels that supply the lungs narrow and their walls thicken, so they can't carry as much blood. Like a kinked garden hose, pressure builds up and backs up. The heart works harder, trying to force the blood through. If the pressure is high enough, eventually the heart can't keep up, and is unable to pump enough blood through the lungs to pick up adequate amounts of oxygen. Patients become tired, dizzy and short of breath. When an underlying cause can't be found, the condition is called primary pulmonary hypertension. When a pre-existing disease such as sickle cell triggers high blood pressure in the lungs, doctors call it secondary pulmonary hypertension because it is secondary to another problem. This is the type of pulmonary hypertension evaluated in the NIH project.

"Secondary pulmonary hypertension develops in most types of hereditary and chronic anemias that are caused by hemolysis, the destruction of red blood cells. This suggests that there is a distinct syndrome of hemolysis-associated pulmonary hypertension, a complication that has been reported with increasing frequency in sickle cell patients," said Dr. Mark Gladwin, pulmonary specialist, NIH Clinical Center and lead investigator of this current research. He pointed out that retrospective studies show a prevalence of pulmonary hypertension ranging from 20-to-40 percent in patients with sickle cell disease.

The research project followed 195 patients, 82 men and 113 women, with an average age of 37, over two years. Doppler echocardiography, a test that uses sound waves to 'see' the heart, was performed on each person to assess their pulmonary-artery pressures. Doppler-defined pulmonary hypertension occurred in 32 percent of the patients. "The 'echo' is a test that is reasonably priced, non-invasive and should be recommended screening for adults with sickle cell disease just as the colonoscopy, cholesterol panel, mammogram, and other tests are. This would save lives and help to minimize a public health problem." said co-investigator Dr. Griffin Rodgers, chief, Clinical Hematology, National Institute of Diabetes and Digestive and Kidney Diseases.

"This is similar to what occurred in the mid-nineties. We saw that use of a transcranial Doppler exam changed the screening and management of pediatric patients with sickle cell disease in that it defined important clinical decision points that successfully led to preventing--or at least improving--the odds of reducing strokes in children and adolescents," added Dr. Rodgers.

Of the 195 individuals evaluated in the current study, 20 percent with pulmonary hypertension died and all but two of the patients without the condition survived. Even patients with mild arterial pressure in the lungs had a high rate of fatality.

Sickle cell treatment continues to improve and people with the disease are living longer. "This," said co-investigator Dr. Oswaldo Castro, Acting Director, Howard University Center for Sickle Cell Disease, "may be why we are seeing such a high prevalence of pulmonary hypertension in sickle cell patients."

Since the study identified those sickle cell patients at the highest risk of death certain therapies targeting pulmonary hypertension could improve survival rates. "Several types of interventional therapies are now available but so far have been tried in only a few sickle cell patients," said Dr. Castro. He referenced inhalants such as oxygen and nitric oxide; blood exchanges through transfusions; and use of vaso-dilator drugs such as Viagra that open the blood vessels or arteries.

Detection of high blood pressure in the lungs may also account for the unexplained or mistakenly explained sudden deaths in adult patients with sickle cell disease. "We see a high frequency of sudden death in those with sickle cell and this study helps to clarify what is causing those fatalities; particularly in the absence of coronary artery disease (hardening of the arteries) as the cause," explained lead investigator Dr. Gladwin.

The co-authors agree that this study's findings represent an opportunity to address a major cause of disability and death in the adult sickle cell disease population--pulmonary hypertension. They believe the research data supports universal screening of individuals with sickle cell disease for this condition and clearly shows the immediate need for clinical trials to further investigate therapies that may combat a serious complication of sickle cell disease that is associated with an ominous outcome.

The research team included collaborators from the Critical Care Medicine Department, Warren Grant Magnuson Clinical Center, NIH; the Cardiovascular Branch, National Heart, Lung, and Blood Institute, NIH; the Hematology Branch, National Institute of Diabetes and Digestive and Kidney Diseases, NIH; and the Center for Sickle Cell Disease, Howard University College of Medicine.