Low blood oxygen may lead to heart defects in children with sickle cell disease

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Children with sickle cell disease who also have lower blood oxygen levels while both asleep and awake are likely to have heart abnormalities, researchers at Washington University School of Medicine in St. Louis and other institutions have found.

Heart problems are fairly common in young adults with sickle cell disease, but physicians don't fully understand why. The researchers demonstrated that lower oxygen saturation in the blood was linked to the heart structure seen in the 44 children studied.

Sickle cell disease is an inherited blood disorder affecting red blood cells, which contain hemoglobin, the substance that carries oxygen from the lungs to all parts of the body. In patients with this disease, red blood cells contain an abnormal type of hemoglobin that causes the normally round, flexible red blood cells to become stiff and sickle- or crescent-shaped. The sickle cells can't pass through tiny blood vessels, which can prevent blood from reaching some tissues and can result in tissue and organ damage, pain and stroke.

In addition, sickle cells are short lived and lead to a shortage of red blood cells and anemia, which make the heart grow bigger because it has to work harder, says Mark C. Johnson, MD, associate professor of pediatrics at Washington University School of Medicine and first author of the study.

In this study, the first to analyze sleep studies and echocardiograms of

children with sickle cell disease, these heart abnormalities were found in the left pumping chamber, or left ventricle, of the children's hearts. The findings included an enlarged left ventricle, called ventricular hypertrophy, and abnormal blood filling of the left ventricle, called diastolic dysfunction. Both are associated with early death in adults with sickle cell disease, but the meanings of the same results in children are unclear.

"This suggests that the beginning of adult heart disease may start in children, but we need to follow these patients longitudinally to strengthen the meaning of the findings," says Michael R. DeBaun, MD, a Washington University sickle cell disease specialist at St. Louis Children's Hospital and senior author of the study, published online in *Blood* First Edition April 8, 2010.

"Many researchers assumed it was the anemia alone that makes the heart enlarge, but this study suggests it's not that simple," Johnson says.

Researchers began the study thinking that the abnormalities in the left ventricle, the heart's main blood-pumping chamber, would be the result of sleep-disordered breathing, such as sleep apnea, commonly found in children with sickle cell disease. Sleep-disordered breathing has previously been associated with left ventricle hypertrophy and with diastolic dysfunction in children and adults. But only about one-fifth of the children had some evidence of obstructive apnea hypopnea, or recurrent episodes of upper airway collapse and obstruction during sleep.

Researchers also thought they would find lower oxygen saturation while patients were sleeping compared to when they were awake. However, the average oxygen saturation while asleep and awake were similar. Only about one-fourth of patients had average oxygen saturation values below normal.

The echocardiograms showed that 46 percent of participants had left ventricle hypertrophy in which the chamber of the left ventricle was enlarged. The research team's analysis showed that for every 1 percent drop in oxygen saturation, there was a measurable increase in the mass of the heart's left ventricle.

"The average oxygen saturation of 97 percent in these children is in a normal range, but the patients with slightly lower levels had enlarged hearts," Johnson says. "A relatively small change in oxygen levels caused a big change in the heart. That's what makes us think there's something under the surface that we don't quite understand yet."

The team also measured an indicator of pulmonary hypertension, or high blood pressure in the lungs, the major cause of death in adults with sickle cell disease. When the pulmonary hypertension level is raised in adults with sickle cell disease, it is a strong predictor of death within 24 months. However, despite the strong association between pulmonary hypertension and sleep abnormalities, no such association was demonstrated in this study, DeBaun says.

Johnson and DeBaun say more sleep and cardiac studies are needed to confirm the association of left ventricle abnormalities with low blood oxygen levels. In the future, the researchers plan to look at other indicators to find potential new therapies to prevent progression of the disease.

More information: Johnson M, Kirkham F, Redline S, Rosen C, Yan Y, Roberts I, Gruenwald J, Marek J, DeBaun M. Left Ventricular Hypertrophy and Diastolic Dysfunction in Children with Sickle Cell Disease are Related to Asleep and Waking Oxygen Desaturation. *Blood* First Edition. Prepublished online April 8, 2010.

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