Sickle Cell Trait May Offer Protective Benefit Against Severe Malaria Symptoms

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Tom Williams, MD, a professor of hemiglobinopathy at Imperial College, London, and KEMRI (Kenya Medical Research Institute) Wellcome Trust, discussed the protective role of sickle cell trait/disease and other hemoglobinopathies against malaria and potential mechanisms at the 10th Sickle Cell in Focus Conference, presented by National Heart, Lung, and Blood Institute and the South Thames Sickle Cell & Thalassemia Network. Research demonstrates that hemoglobin AS, CC, and AC genotypes — along with homozygous and heterozygous thalassaemia — provide significant protection from severe malaria syndromes. However, the degree of protection provided differed significantly among the haemoglobinopathies. While sickle cell trait and sickle cell disease appear to confer a progressive survival advantage against malaria infection (infection with HbAS > infection with HbSS) in endemic regions, homozygous sickle cell appears to play a key role in malaria-related morbidity and mortality. Heterozygosity, however, confers significantly reduced risk of malaria-related morbidity and mortality. A better understanding of the resistance to malaria associated with hemoglobinopathies could lead to identification of the mechanisms of malaria pathogenesis and immunity and ultimately to improved prophylaxis and therapies.

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In a related presentation, Hans Ackerman, MD, DPhil, an investigator at the, discussed the impact of iron availability on malaria and sickle cell disease severity. Iron deficiency is associated with lower incidences of parasitemia and severe malaria. Evidence suggests that universal iron supplementation may be linked to increased death and hospitalization. The risk of malaria is increased with iron supplementation. Supplementation appears only to help children who are iron-deficient and anemic. While the data for an association between iron status and sickle cell disease

is sparse, it suggests that iron deficiency may result in less sickling. Iron repletion may exacerbate symptoms in patients with sickle cell disease.. Animal studies show that iron-deficiency coupled with sickle cell disease is associated with decreased RBC turnover.

Deepika Darbari, MBBS, MS, of Children's National Medical Center, said that inflammation caused by sickle cell pathobiology plays a crucial role in paint experience by patients with acute and chronic sickle cell disease. In addition, chemical and structural changes, which occur in the presence of pain and injury (in conjunction with environmental and genetic factors) lead to receptor and neurotransmitter changes changes in the brain (neuroplasticity). Studies support the role of peripheral and central sensitization in sickle cell pain, meaning that patients with sickle cell disease do experience pain differently. Mechanistic therapies are being developed to treat pain associated with sickle cell disease, she concluded.

The meeting also highlighted the role of genotyping for variant antigens in sickle cell disease — particularly RHD and RHCE; and evidence for coagulation activation contributing to sickle cell disease pathophysiology.