

## **Review of mechanisms of brain injury identified in severe malaria from 2010-2020**

Minal Patel<sup>1</sup>, Adnan Gopinadhan<sup>2,3</sup>, Katrina Co<sup>2</sup>, Amy Belvin<sup>4</sup>, Robert O. Opoka<sup>5</sup>, Paul Bangirana<sup>5</sup>, Dibyadyuti Datta<sup>2</sup>, Chandy C. John<sup>2</sup>

<sup>1</sup>*Indiana University School of Medicine, Indianapolis, Indiana*, <sup>2</sup>*Ryan White Center for Pediatric Infectious Disease and Global Health, Department of Pediatrics, Indiana University School of Medicine, Indianapolis, Indiana*, <sup>2</sup>*Department of Microbiology and Immunology, Indiana University School of Medicine, Indianapolis, Indiana*, <sup>3</sup>*Department of Paediatrics and Child Health, Makerere University, Kampala, Uganda*, <sup>4</sup>*Ruth Lilly Medical Library, Indiana University School of Medicine, Indianapolis, Indiana* <sup>5</sup>*Department of Psychiatry, Makerere University, Kampala, Uganda*

### **Background:**

Severe malaria manifests as various conditions with severe malarial anemia being the most common and cerebral malaria being the most severe and affecting over 200,000 children annually. A 2010 review highlighted blood brain barrier degradation and decreased cerebral perfusion as contributors to the long-term behavioral, cognitive, and neurological sequelae of severe malaria. Since then, new research has identified various surface marker proteins and cytokines/chemokines playing a role in vascular changes and inflammation that progresses to acute kidney injury, retinopathy, and seizures. Our goal is to summarize the updated research and provide further insight into the mechanisms of brain injury and the outcomes that follow cerebral malaria.

### **Project Methods:**

Hypotheses on future areas of study from the 2010 review were used to generate an outline for the updated review. Search strategies using the PubMed database were developed so that all relevant primary articles pertaining to human (pediatric and adult), murine, and in vitro studies done from 2010-2020 could be identified. The articles were then sorted and inputted into EndNote to generate a library. Review articles, case reports, and articles discussing the treatment of malaria were excluded from this index.

### **Results:**

88 articles remarking on vasculopathy, 88 on leukocytes, 114 on cytokines/chemokines, 11 on seizures, 56 on acute kidney injury, and 35 on retinopathy have been identified as promising literature for this review. The results suggest that infected individuals have increased endothelial activation which promotes red blood cell adherence to vasculature and edema. This reduces blood flow to the brain, kidneys, and eyes and causes injury to the organs.

### **Conclusion and Potential Impact:**

The EndNote library contains current literature on the mechanisms of brain injury secondary to severe malaria, which will be used to write a review article and identify new areas of research to further our understanding of severe malaria pathogenesis and how to target treatments.