Common enzyme deficiency may hinder plans to eradicate malaria

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In malaria-endemic countries, 350 million people are predicted to be deficient in an enzyme that means they can suffer severe complications from taking primaquine, a key drug for treating relapsing malaria, according to a study funded by the Wellcome Trust and published in this week's *PLOS Medicine*.

This finding is important as primaquine is recommended in the global action plan to eliminate malaria and is the only drug to prevent malaria relapse. The benefits of implementing a treatment program with this drug need to be weighed against the potential harm to a substantial proportion of the population (up to 8%) who may have G6PD deficiency: a genetic defect reducing glucose-6-phosphate dehydrogenase enzyme activitiy. Individuals with G6PD deficiency who are given primaquine can experience a severe complication – the breakdown of their red blood cells (hemolysis).

The authors from Indonesia, Kenya, the Philippines, and the United Kingdom, led by Rosalind Howes from the University of Oxford, reached these conclusions by inputting information about the frequency of G6PD deficiency from community surveys into a geostatistical model. Using the model, the authors predicted that G6PD deficiency is widespread across malaria-endemic regions, with the lowest frequencies in North and South America and the highest frequency in tropical Africa and the Arabian Peninsula.

Dr Howe explains: "Malaria control and elimination are a top priority on

the global health agenda. Yet, a key drug to help achieve this goal remains too dangerous for widespread use. We have developed a map of this risk factor, G6PD deficiency, and find it to be very common across many malaria endemic regions. Much work remains to be done to fully understand this disease, notably its genetic diversity."

The authors found that the predicted frequency of G6PD deficiency varied considerably over relatively short distances in many areas but the overall frequency was 8% in malaria-endemic countries, corresponding to about 350 million affected individuals. In countries that are currently planning to implement malaria elimination programs, the frequency was 5.3%, corresponding to 100 million affected individuals.

When the authors took the severity of the G6PD deficiency (the more severe the deficiency, the higher the risk of hemolysis), they found that the greatest risk was across Asia, where severe G6PD variants are commonly inherited.

The authors say: The prominence of G6PD deficiency represents a barrier to current options for malaria elimination therapy."

They continue: "The complexity and diversity of both malaria epidemiology and G6PD deficiency mean that no single solution will be applicable for ensuring safe and effective primaquine treatment."

More information: Howes RE, Piel FB, Patil AP, Nyangiri OA, Gething PW, et al. (2012) G6PD Deficiency Prevalence and Estimates of Affected Populations in Malaria Endemic Countries: A Geostatistical Model-Based Map. PLoS Med 9(11): e1001339. doi:10.1371/journal.pmed.1001339

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