Competitive facilitation of drug-resistant *Plasmodium falciparum* malaria parasites in pregnant women who receive preventive treatment

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Abstract

Intermittent preventive treatment in pregnancy (IPTp) is used to prevent *Plasmodium falciparum* malaria. However, parasites resistant to the IPTp drug sulfadoxine-pyrimethamine (SP) have emerged worldwide, and infections with mixed resistant and susceptible parasites are exacerbated by pyrimethamine in mice. In a prospective delivery cohort in Muheza, Tanzania, we examined the effects of SP IPTp on parasite resistance alleles, parasite diversity, level of parasitemia, and inflammation in the placenta. IPTp use was associated with an increased fraction of parasites carrying the resistance allele at DHPS codon 581, an increase in the level of parasitemia, and more intense placental inflammation. The lowest mean level of parasite diversity and highest mean level of parasitemia occurred in women after recent IPTp use. These findings support a model of parasite release and facilitation, whereby the most highly resistant parasites out-compete less fit parasite populations and overgrow under drug pressure. Use of partially effective anti-malarial agents for IPTp may exacerbate malaria infections in the setting of widespread drug resistance.