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Plasmodium falciparum treated with artemisinin-based combined therapy exhibits enhanced mutation, heightened cortisol and TNF-α induction

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The artemisinin-based combined therapy (ACT) post-treatment illness in Plasmodium falciparum-endemic areas is characterized by vague malaria-like symptoms. The roles of treatment modality, persistence of parasites and host proinflammatory response in disease course are unknown. We investigated the hypothesis that ACT post-treatment syndrome is driven by parasite genetic polymorphisms and proinflammatory response to persisting mutant parasites. Patients were categorized as treated, untreated and malaria-negative. Malaria positive samples were analyzed for Pfcrt, Pfmdr1, K13 kelch gene polymorphisms, while all samples were evaluated for cytokines (TNF-α, IL-12p70, IL-10, TGF-β, IFN-γ) and corticosteroids (cortisol and dexamethasone) levels. The treated patients exhibited higher levels of parasitemia, TNF-α, and cortisol, increased incidence of parasite genetic mutations, and greater number of mutant alleles per patient. In addition, corticosteroid levels declined with increasing number of mutant alleles. TGF-β levels were negatively correlated with parasitemia, while IL-10 and TGF-β were negatively correlated with increasing number of mutant alleles. However, IL-12 displayed slight positive correlation and TNF-α exhibited moderate positive correlation with increasing number of mutant alleles. Since post-treatment management ultimately results in patient recovery, the high parasite gene polymorphism may act in concert with induced cortisol and TNF-α to account for ACT post-treatment syndrome. In conclusion, the ACT-meted-syndrome consists of post-treatment malaria-like-illness, enhanced genetic polymorphism in parasite that may not be effective phenotypes, and proinflammatory conditions accompanied by regulatory cytokine impairment.

Biography

Anthony A Azenabor is full professor at the University of Wisconsin-Milwaukee and an expert in Infection and Immunity, he has approached his research by explaining the impact of infection on host immune system, relying on my knowledge of Molecular Biochemistry as a major tool. His current research is aimed at providing greater insights into mechanisms involved in innate immune function during stimulation by both physiologic and infectious agents. His finding have contributed to the concept that products of activation by therapeutic interventions and the infectious agents play combined roles in the activation, wholly or in part, of host defence against pathogens and other challenges.

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