

Epidemiology

1. What is the real incidence of severe disease in population-based studies in Latin America?
2. Is the incidence of severe disease similar in distinct epidemiological scenarios? And what is the impact of the health system organization on this severity?
3. What is the prognosis and fatality rate of severe disease in hospitalized and non-hospitalized patients?
4. What is the role of host genetics (e.g. Duffy genotypes, G6PD deficiency) upon severity?

Clinical aspects

1. Do the WHO criteria for severe *P. falciparum* malaria also apply for *P. vivax* severe disease?
2. Which clinical complications are able to predict death?
3. What is the contribution of co-morbidities to severe disease?
4. What is the contribution of concurrent infections (bacterial, viral, fungal, parasitic) to severe disease?
5. Are there specific severity presentation in some groups, e.g. pregnant women and children?
6. Which are the bad prognostic findings in obstetric ultrasounds in pregnant women with malaria?
7. What is the burden of clinical complications related more to drugs' side effects?

Pathogenesis

1. Which are the microscopic findings of autopsies from patients who died with the diagnosis of vivax infection?
2. Do all the clinical complications, classified as 'severe', share the same mechanisms of disease?
3. Is severe disease linked to the existing evidence of *ex vivo* cytoadhesion of *P. vivax* infected RBCs? What triggers endothelial activation?
4. Which are the best biomarkers for severity?

Therapeutic aspects

1. Is clinical severity linked to CQ-resistance?
2. What should be the standard-of-care specific treatment for severe patients in areas where CQ-resistance is not high?
3. Antibiotics should be used systematically in which severe complications?
4. What type of adjunctive treatment should be initiated?