

Changing Pattern of Vivax Malaria

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Editorial

Malaria, since the history of mankind, has proved to be a disease with extreme consequences. It has had a restriction on the overall progress of mankind not only health but cultural and socioeconomic wellbeing in the tropical, subtropical and monsoon prone zones of the world. More than half of the world's population, in 104 countries, is exposed to malaria. Out of this 22% people are living under high risk conditions. Globally the population at risk for malaria accounts to 3.3 billion. The suspected malaria cases are estimated to be about 200-300 million every year of which 781000 deaths were recorded during 2010 [1].

Malaria has a tremendous impact on premature death and disability which on a population or national level poses barriers to economic growth and development [1]. The magnitude of the malaria problem is compounded by that young children are the most affected. Worldwide, 38% of incidence and 85% of deaths are concerned with children under the age of five years [2]. The dreaded disease is difficult to eradicate and its control is possible only with coordinated efforts of the general public, healthcare personnel and government agencies.

Malaria is a protozoal disease caused by infection with parasites of genus *Plasmodium*, earlier only 4 species of *Plasmodium* were known to cause malaria in humans: *P. falciparum*, *P. vivax*, *P. malariae* and *P. ovale*, but in 2004 *P. knowlesi* (a primate malaria species) was also shown to cause human malaria. Malaria is transmitted to man by bite of certain species of infected female Anopheline mosquito. Out of these *Plasmodium vivax* and *Plasmodium falciparum* account for the greatest prevalence in the world. Over the past decade there has been a considerable decline in incidence of *P. falciparum* infection as reported in different parts of the World. Nearly 38 countries have shown more than 50% decline in *P. falciparum* cases [3]. In Asian region, *P. vivax* is now emerging as the dominant *Plasmodium* species, with chloroquine resistance starting to spread [4].

Vivax malaria has long been considered to have a benign course with frequent relapses while falciparum malaria is mostly responsible for severe complications and associated mortality. Because of nature of the problems, most of the literature published on malaria focuses on *P. falciparum* and much less on *P. vivax*.

Recent evidence from all over the world shows that *Plasmodium vivax* malaria is clinically less benign than has been commonly believed and has been challenged by numerous reports of symptoms and signs of severe disease and even deaths due to *P. vivax* mono-infections. Almost all the complications of severe malaria like cerebral malaria, shock, acute lung injury, ARDS, bleeding diathesis, acute kidney injury are now being reported in vivax mono-infection, also the haematological complications like thrombocytopenia, anaemia, pancytopenia and leucopenia [5,6].

Profound thrombocytopenia is a well-recognized complication of falciparum malaria but has been less well described in vivax malaria. Most studies done in 21st century consistently shows association of thrombocytopenia in vivax malaria. Sometimes thrombocytopenia can be severe enough to cause spontaneous bleeding even in absence of DIC [7].

The parasite index in vivax malaria is no way near falciparum malaria. Still anemia can be severe enough to require blood transfusions. Clearly this anemia is not just due to destruction of RBCs but destruction of non-infected RBCs too. The possible mechanisms include increased fragility, invasion and destruction of reticulocytes, pooling of RBCs in spleen and increased cytokines production [7,8].

Vivax malaria usually involves lungs and cough is a common manifestation even in benign disease. Malaria in its severe form can cause acute lung injury (ALI) and acute respiratory distress syndrome. However this is less commonly seen in children as compared to adults [9]. The main pathophysiologic mechanism behind respiratory distress in malaria is increased alveolar capillary permeability leading to intravascular fluid loss into the lungs.

CNS manifestations in form of coma, although rare, but is increasingly recognised in vivax malaria. Some of the cases may be due to co-infection with falciparum malaria. The cytoadherence is thought to be central to this phenomenon but other mechanisms could also be responsible. Metabolic derangements, microvascular pathologies in CNS and DIC could be the other possible mechanisms [9,10]

The key difference between the pathogenesis of *P. falciparum* and *P. vivax* is the number of RBCs parasitized. *P. falciparum* invades RBCs both young and old. Vivax on the other hand infects mostly young RBCs. Consequently *P. falciparum* is responsible of high parasite burden and the parasite burden of *P. vivax* is usually less than 2%. The high parasite index does explain most of the severe manifestations of *P. falciparum*. The red cell selectivity index in vivax malaria was found to be significantly greater than that in falciparum malaria at a comparable parasitaemic index. However that still does not offer explanation for severity increasingly seen in vivax malaria too. It has been observed that the inflammatory response seen in vivax malaria is more than the falciparum for the same amount of parasite load. Hence vivax malaria can mount a reasonably higher degree of inflammatory response even with lower parasite index. The reasons for this phenomenon are not very clear. The explanations offered range from increased cytokine production to leucocyte aggregation, endothelial activation, altered thrombosis and comorbidities to name a few. One phenomenon seen even in clinically milder form of vivax malaria is the consistent presence of thrombocytopenia. The explanation offered is the increased peripheral destruction due to microvascular pathologies [11]. Again a consequence of increased inflammatory response.

Although *P. vivax* resistance to chloroquine is increasingly reported, it is still sensitive to an extent that it stays as the drug of choice for the treatment. However looking at the future scenario, this problem of resistance is only going to increase. And to couple it with the severity of disease, we might be looking at the disaster in making. Despite our better understanding of the disease there are still many unanswered questions. Unfortunately the amount of research going in is clearly insufficient. The current focus on malaria research is mainly focused on either development of a safe and effective vaccine or searching] for new drugs in response to the emerging resistance. But at the same time, it is also important to understand the pathophysiologic mechanisms of the disease. We still do not know answers to the reason why vivax malaria is no more a benign disease. Better understanding of the disease and its manifestations will result in the better management of complications and in reduction of morbidity and mortality.

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