The Changing Scenario of Malaria in India

FD Dastur

Malaria is a disease of tropical and subtropical climates and has been entrenched in India for countless years. Recent data suggests the burden of disease may actually be increasing. Official number of cases for 2009 in India was 1.6 million with 10,000 deaths. These figures have been challenged and deaths between 125000 – 277000 based on verbal autopsy reports have been suggested. Whatever the exact numbers the picture appears at odds with some other Asian and African countries which have seen a decline in morbidity and mortality probably due to more political commitment and the benefits from international funding agencies such as Roll Back Malaria.

Malaria like other infectious diseases is influenced in its behaviour by external forces. Recent history shows that Plasmodium falciparum incidence in India has increased from 14% in 1970 to over 50% in 2009. Chloroquine resistance in P. falciparum arose in S.E. Asia during the Vietnam war (1968 – 1973) when chloroquine was used to treat malaria. At that stage the parasite was confined into a highly malarious zone and Chloroquine prophylaxis may be presumed to have been erratic. Resistance then spread westward to enter India’s eastern borders and slowly spread countrywide. This heightened the challenge that India’s large geographical area and population already posed to malaria control. Rapid urbanization, and labour migration also played their part. Drug therapy for Chloroquine resistant P. falciparum was changed to pyrimethamine – sulfadoxine or to quinine for severe disease. Artemisinin the danger of monotherapy in relation to drug resistance was realized and artemisinin combination therapy (ACT) advocated. This combined a long acting antimalarial with short acting artemisinin.

The mosquito vectors of Plasmodia have also played a significant role in furthering the spread of P. falciparum malaria. Anopheles culicifacies and Anopheles fluviatilis are the two important vectors in rural India and both now are resistant to many insecticides. Both species flourish during the monsoon and account for malaria outbreaks which have increased in frequency since the 1990s. They invade construction sites, irrigation areas and wherever industrialization is occurring. In cities Anopheles Stephensi breeds efficiently in fresh water storage tanks and in collections of rain water and at construction sites. The Urban Malaria scheme was launched in 1970 to distribute insecticide treated bed nets, to carry out indoor residual spraying of dwellings, and to give antimalarials to infected persons. However a recent review of its functioning in selected pilot areas did not find the scheme to be working efficiently.

In the past five years the scenario shows an unexpected development and it is Plasmodium vivax that springs the surprise. Known for long as benign tertian malaria on the basis that it infects only young red cells with a resultant parasite load that rarely exceeds 2 percent the disease could usually be managed on an outpatient basis. P. vivax though does have certain individual features of its own. Gametocytes are produced early in the disease, often before drugs are started, thus making for more efficient transmission than P. falciparum. Hypnozoites in the liver can cause multiple disease relapses which occur in about 30% of cases without specific treatment. The only effective drug is Primaquine, and there is strong evidence from Indonesia and Oceania of increasing Primaquine resistance. In India we are also beginning to see relapses when standard dosing of 7.5 mg bid x 14 d is used regardless of patient body weight. Complications regularly associated with P. vivax are thrombocytopenia, anaemia and occasionally splenic rupture but mortality in the absence of patient comorbidities remains low. Now this is changing. Patients with P. vivax infection have developed acute lung injury, acute kidney injury, cerebral malaria, severe jaundice, shock and pulmonary oedema. Initially these were assumed to be mixed infections but now with molecular diagnostics and PCR studies that bogy has been removed. Kocher and his group from Bikaner, Rajasthan deserve credit for being the first to draw attention to severe P. vivax infection from their part of the country in a number of publications over the last decade. It is also why the article in this issue of the Journal assumes significance as it compares the complications encountered in P. vivax malaria to that seen in P. falciparum infections in a large municipal hospital in Mumbai during the monsoon months. The authors point out there was no evidence to suggest Chloroquine resistance but even so severe P. vivax cases received ACT in addition.

Complications in severe malaria are seen as either sequestration (cytoadherence and rosetting) related such as cerebral malaria, or non sequestration related such as anaemia and thrombocytopenia. Sequestration has not been thought to be part of the pathophysiology of P. vivax infection but with the above mentioned complications that assumption must now be challenged. Laboratory and clinical studies are on going and certain facts are emerging. For an equal parasite load P. vivax excites a greater inflammatory response than does P. falciparum. In clinical studies in the Amazon region of Brazil immunopathological events were studied in P. vivax infections. Plasma levels of tumour necrosis factor (TNF) and interferon – gamma (IFN – gamma) were increased and showed a linear trend with worsening of disease and resolution with recovery. Strong proinflammatory responses may lead to a cytokine imbalance during infection it is hypothesized but further understanding is awaited.

These are testing times for P. vivax but if the coming year shows it is still ‘punching above its weight’ it should encourage large scale multicentre studies to better define the geography, temporal profile, demographics, and pathophysiology of this fascinating change in character of P. vivax infection.

References