Study in Myanmar confirms artemisinin-resistant malaria close to border with India

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The spread of malaria parasites that are resistant to the drug artemisinin - the frontline treatment against malaria infection - into neighbouring India would pose a serious threat to the global control and eradication of malaria. If drug resistance spreads from Asia to the African sub-continent, or emerges in Africa independently as we've seen several times before, millions of lives will be at risk.

The collection of samples from across Myanmar and its border regions was led by Dr Kyaw Myo Tun of the Defence Services Medical Research Centre, Napyitaw, Myanmar and coordinated by the Mahidol-Oxford Tropical Medicine Research Unit (MORU) in Bangkok, Thailand. The researchers examined whether parasite samples collected at 55 malaria treatment centres across Myanmar carried mutations in specific regions of the parasite's kelch gene (K13) - a known genetic marker of artemisinin drug resistance. The team confirmed resistant parasites in Homalin, Sagaing Region located only 25km from the Indian border.

"Myanmar is considered the frontline in the battle against artemisinin resistance as it forms a gateway for resistance to spread to the rest of the world," says Dr Charles Woodrow from the Mahidol-Oxford Tropical Medicine Research Unit and senior author of the study at Oxford University. "With artemisinins we are in the unusual position of having molecular markers for resistance before resistance has spread globally. The more we understand about the current situation in the border regions, the better prepared we are to adapt and implement strategies to overcome the spread of further drug resistance."

The team obtained the DNA sequences of 940 samples of malaria infections (known as *Plasmodium falciparum* malaria parasites) from across Myanmar and neighbouring border regions in Thailand and Bangladesh between 2013 and 2014. Of those 940 samples, 371 (39%) carried a resistance-conferring K13 mutation.

"We were able to gather patient samples rapidly across Myanmar, sometimes using discarded malaria blood diagnostic tests and then test these immediately for the K13 marker, and so generate real-time information on the spread of resistance" said Dr Mallika Imwong, research lead for the laboratory analysis at Mahidol University's Faculty of Tropical Medicine in Bangkok, Thailand.

Using this information, the researchers developed maps to display the predicted extent of artemisinin resistance determined by the prevalence of K13 mutations. The maps suggest that the overall prevalence of K13 mutations was greater than ten per cent in large areas of the East and North of Myanmar, including areas close to the border with India.

"The identification of the K13 markers of resistance has transformed our ability to monitor the spread and emergence of artemisinin resistance," says Professor Philippe Guerin, Director of the Worldwide Antimalarial Resistance Network (WWARN) and co-author of the study. "However, this study highlights that the pace at which artemisinin resistance is spreading or emerging is alarming. We need a more vigorous international effort to address this issue in border regions."

Professor Mike Turner, Head of Infection & Immunobiology at the Wellcome Trust, said "Drug resistant malaria parasites in the 1960s originated in Southeast Asia and from there spread through Myanmar to India, and then to the rest of the world where it killed millions of people. The new research shows that history is repeating itself with parasites resistant to artemisinin drugs, the mainstay of modern malaria treatment, now widespread in Myanmar. We are facing the imminent threat of resistance spreading into India, with thousands of lives at risk."

Gathering near 'real-time' information on malaria drug resistance is critical to help predict the geographic routes of drug resistance and inform national and regional patient treatment strategies. Mapping the spread together with a more systematic review and revision of medicine dosing strategies, especially for vulnerable groups such as children and pregnant women, will help to preserve and ultimately prolong the life-span of these life-saving medicines. It is only through researchers, policy makers, doctors and funding partners working collaboratively that the global health community can minimise the threat of resistance and safeguard the vital public health gains we have made in malaria control and elimination.

More information: Tun et al. Spread of artemisinin-resistant Plasmodium falciparum in Myanmar: a cross-sectional survey of the K13 molecular marker. *Lancet Infectious Diseases*. Published online February 20 2015. www.thelancet.com/journals/lan … (15)70032-0/abstract

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