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Spatio-temporal distribution and hotspots of *Plasmodium knowlesi* infections in Sarawak, Malaysian Borneo

Nur Emyliana Yunos¹, Hamidi Mohamad Sharkawi², King Ching Hii³, Ting Huey Hu¹, Dayang Shuaisah Awang Mohamad¹, Nawal Rosli¹, Tarmiji Masron⁴, Balbir Singh¹ & Paul Cliff Simon Divis¹✉

Plasmodium knowlesi infections in Malaysia are a new threat to public health and to the national efforts on malaria elimination. In the Kapit division of Sarawak, Malaysian Borneo, two divergent *P. knowlesi* subpopulations (termed Cluster 1 and Cluster 2) infect humans and are associated with long-tailed macaque and pig-tailed macaque hosts, respectively. It has been suggested that forest-associated activities and environmental modifications trigger the increasing number of knowlesi malaria cases. Since there is a steady increase of *P. knowlesi* infections over the past decades in Sarawak, particularly in the Kapit division, we aimed to identify hotspots of knowlesi malaria cases and their association with forest activities at a geographical scale using the Geographic Information System (GIS) tool. A total of 1064 *P. knowlesi* infections from 2014 to 2019 in the Kapit and Song districts of the Kapit division were studied. Overall demographic data showed that males and those aged between 18 and 64 years old were the most frequently infected (64%), and 35% of infections involved farming activities. Thirty-nine percent of Cluster 1 infections were mainly related to farming surrounding residential areas while 40% of Cluster 2 infections were associated with activities in the deep forest. Average Nearest Neighbour (ANN) analysis showed that humans infected with both *P. knowlesi* subpopulations exhibited a clustering distribution pattern of infection. The Kernel Density Analysis (KDA) indicated that the hotspot of infections surrounding Kapit and Song towns were classified as high-risk areas for zoonotic malaria transmission. This study provides useful information for staff of the Sarawak State Vector-Borne Disease Control Programme in their efforts to control and prevent zoonotic malaria.

Malaria, a mosquito-borne disease, is widely distributed in the tropical and subtropical regions, with more than 400,000 annual deaths reported¹. Zoonotic malaria by the simian parasite *Plasmodium knowlesi* became prominent since the large focus of cases reported in Kapit division of Sarawak state, Malaysian Borneo almost two decades ago². Knowlesi malaria have been reported in countries across Southeast Asia at low frequency, however, highest prevalence of clinical cases has mainly occurred in Malaysian Borneo³. According to the Ministry of Health Malaysia, the prevalence of indigenous malaria caused by human parasites *P. vivax*, *P. falciparum*, *P. malariae* and *P. ovale* has shown a remarkable decrease while knowlesi malaria cases have continuously shown an increasing trend with 509 annual cases reported in 2010, to between 1813 and 4124 cases from 2012 to 2020⁴ (Ministry of Health Malaysia, unpublished data). Malaysia is listed by the WHO as one of the countries that has substantially progressed in eliminating malaria by the year 2020¹. However, zoonotic malaria cases caused by *P. knowlesi* are excluded from the definition of malaria elimination by WHO, which focuses on only the human *Plasmodium* species^{1,5,6}.

The malaria-free status by WHO is confirmed if zero incidence of indigenous cases for at least three consecutive years, denoting full interruption of local malaria by *Anopheles* mosquitoes. Nonetheless, certification

¹Malaria Research Centre, Faculty of Medicine and Health Sciences, Universiti Malaysia Sarawak, Kota Samarahan, Sarawak, Malaysia. ²Ministry of Health Malaysia, Kapit Divisional Health Office, Kapit, Sarawak, Malaysia. ³Ministry of Health Malaysia, Kapit Hospital, Kapit, Sarawak, Malaysia. ⁴Centre for Spatially Integrated Digital Humanities, Faculty of Social Sciences and Humanities, Universiti Malaysia Sarawak, Kota Samarahan, Sarawak, Malaysia. ✉email: pcsimon@unimas.my