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Spatial analyses of *Plasmodium knowlesi* vectors with reference to control interventions in Malaysia

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Abstract

Background Malaria parasites such as *Plasmodium knowlesi*, *P. inui*, and *P. cynomolgi* are spread from macaques to humans through the Leucosphyrus Group of *Anopheles* mosquitoes. It is crucial to know the distribution of these vectors to implement effective control measures for malaria elimination. *Plasmodium knowlesi* is the most predominant zoonotic malaria parasite infecting humans in Malaysia.

Methods Vector data from various sources were used to create distribution maps from 1957 to 2021. A predictive statistical model utilizing logistic regression was developed using significant environmental factors. Interpolation maps were created using the inverse distance weighted (IDW) method and overlaid with the corresponding environmental variables.

Results Based on the IDW analysis, high vector abundances were found in the southwestern part of Sarawak, the northern region of Pahang and the northwestern part of Sabah. However, most parts of Johor, Sabah, Perlis, Penang, Kelantan and Terengganu had low vector abundance. The accuracy test indicated that the model predicted sampling and non-sampling areas with 75.3% overall accuracy. The selected environmental variables were entered into the regression model based on their significant values. In addition to the presence of water bodies, elevation, temperature, forest loss and forest cover were included in the final model since these were significantly correlated. *Anopheles* mosquitoes were mainly distributed in Peninsular Malaysia (Titiwangsa range, central and northern parts), Sabah (Kudat, West Coast, Interior and Tawau division) and Sarawak (Kapit, Miri, and Limbang). The predicted *Anopheles* mosquito density was lower in the southern part of Peninsular Malaysia, the Sandakan Division of Sabah and the western region of Sarawak.

Conclusion The study offers insight into the distribution of the Leucosphyrus Group of *Anopheles* mosquitoes in Malaysia. Additionally, the accompanying predictive vector map correlates well with cases of *P. knowlesi* malaria. This research is crucial in informing and supporting future efforts by healthcare professionals to develop effective malaria control interventions.

Keywords *Anopheles*, Distribution, Leucosphyrus group, Predictive vector map, Malaysia

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Background

Malaria is a significant global health concern that continues to cause fatalities and illnesses, especially in tropical areas [1]. The abundance of mosquito vectors, which thrive in suitable environments, such as those characterized by high humidity, precipitation, temperature and climate seasonality, contributes to the high incidence rate of malaria [2]. Although synthetic insecticides have been utilized to control these vectors, the growing resistance of malaria vectors to chemicals poses a threat to malaria prevention [2, 3]. Therefore, there is a need for more effective control measures to address this issue.

Although *Plasmodium knowlesi* has become more prevalent in recent years, the emergence of *Plasmodium cynomolgi* and *Plasmodium inui* as zoonotic malaria in Southeast Asia has complicated measures aimed at malaria elimination [4–6]. The WHO reports that countries will not achieve malaria elimination status if the number of *P. knowlesi* cases remains high [7]. Studies have identified several mosquito species from the Leucosphyrus Group of the genus *Anopheles*, including *An. cracens* [8, 9], *An. latens* [10], *An. balabacensis* [11, 12], and *An. introlatus* [13], that can transmit *P. knowlesi* to humans.

Most strategies for controlling malaria have focused on eliminating the disease in humans. This is understandable since humans account for the majority of malaria cases worldwide. However, the idea that simian malaria would rarely spill over into humans, proposed in the 1960s, is now outdated [14]. Recent developments have shown that zoonotic malaria is now a significant public health concern in Southeast Asia. Therefore, before declaring malaria eradication status, it is crucial to reconsider the threat of simian malaria and establish monitoring and control strategies [15–18]. Hence, mapping the distribution of simian malaria vectors in Southeast Asia is essential to the implementation of effective surveillance and control measures to eliminate the disease.

Comprehending the spatial and temporal pattern of simian malaria vectors is crucial, as it helps identify hot-spot areas for vector abundance and allocating resources. Many studies have effectively used global geospatial techniques in mosquito environmental research [19–22]. These tools have also helped predict habitat suitability, which aids in designing optimal mosquito vector control strategies based on precise spatial and temporal information databases [23–25]. Geospatial mapping has the potential to identify larval habitats covering a large geographic area, which may be difficult or impossible to obtain through field surveys [20, 26].

Due to deforestation and changes in land use, certain *Anopheles* species from the Leucosphyrus Group have become more prevalent in farms and villages [27, 28].

However, there is still a need for high-quality knowledge on the distribution of these vectors throughout Malaysia. The spatial distribution of simian malaria vectors is crucial to determining effective vector control strategies but, unfortunately, there is currently a lack of information on their distribution throughout the country. Understanding the transmission patterns and geographical distribution of simian malaria parasites in Malaysia is essential for developing efficient disease control strategies and identifying how ecologies affect the risks of simian malaria. Therefore, this study aims to create a geographical distribution map and a predictive risk map based on the ecology of specific vectors of *P. knowlesi*. This information will enable possible interventions that can be used for vector control.

Methods

Data search

Relevant information on the Leucosphyrus Group of *Anopheles* mosquitoes was obtained through a combination of: (i) an extensive search of published articles on the *Anopheles leucosphyrus* sensu lato (*A. leucosphyrus* s.l.) mosquitoes between 1957 and 2021; (ii) mosquito sample collections carried out in the course of the present study from June 2019 until January 2021 in Malaysia (Fig. 1), the details of which regarding the sample collection are described in a previous study [29]; and (iii) direct contacts with district officers for *Anopheles* collection sites coordinates or unpublished research data were used for the spatial analysis. Online platform databases, such as PubMed, Medline and Google Scholar, were searched used to identify relevant studies on distribution of the simian malaria vector. We also compiled information from gray literature, such as hard copies of old publications, reports, thesis and dissertations pertinent to the research.

Geo-positioning procedures

The surveyed geographic coordinates were determined using electronic resources, including GeoNet Names Server (<http://earth-info.nga.mil>), Wikimapia (<http://www.wikimapia.org>) and Google Earth (<http://www.earth.google.com>), which are freely available online. The identified location from one source was cross-checked against the other sources to confirm the consistency of the coordinates. Each collection area's coordinates were recorded using the Google Maps coordinate system. The recorded coordinates were then transferred to Microsoft Excel 2016 (Microsoft Corp., Redmond, WA, USA) to compile all the data for further analysis. All digital data and geographical coordinate were synchronized using the World Geodetic System (WGS1984; <https://gisgeography.com/wgs84-world-geodetic-system/>), which served