

Human Behavior in Plasmodium knowlesi Malaria Infection

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P. knowlesi is a zoonotic disease transmitted by the *Anopheles* mosquito, which harbors the *Plasmodium* parasite. Previously, the disease was believed to occur only among the *Macaca fascicularis* and *M. nemestrina* monkeys, found largely in southeast Asia.

Plasmodium knowlesi

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intervention

1. Introduction

P. knowlesi is a zoonotic disease transmitted by the *Anopheles* mosquito, which harbors the *Plasmodium* parasite [1]. Previously, the disease was believed to occur only among the *Macaca fascicularis* and *M. nemestrina* monkeys [1], found largely in southeast Asia [1]. In 2004, *P. knowlesi* infection was detected in a large section of the community in Sarawak, Malaysia [1]. Despite the success of malaria elimination programs worldwide [2][3][4], these zoonotic infections have been observed to be exponentially increasing among humans in Sabah, Malaysia [2], and nearby countries such as Indonesia [5][6], Vietnam [7][8], and Cambodia [9]. Patients experienced symptoms such as fever, myalgia, and headache, and in severe cases, kidney complications and fatalities [1][2].

The vectors of *P. knowlesi* are *Anopheles* mosquitoes of the *Leucospyrus* group [10]. There is heterogenicity in vector species across geographical regions in southeast Asia (SEA). For example, the species, *Anopheles balabacensis*, from the *Leucospyrus* complex, is widely distributed in east Malaysia, the Philippines, and Indonesia [10]. *Anopheles cracens* from the *Dirus* complex is found in Indonesia, West Malaysia, and Thailand, while *Anopheles dirus* is the primary vector in Cambodia, Laos, Thailand, Vietnam, and China [10].

The distribution of both adult mosquitoes and breeding sites provides important vector control evidence. These forest-dwelling vectors favor humid and covered forest and breed in temporary habitats such as puddles, ground holes, stream margins, and wheel tracks. The *Anopheles balabacensis* favors secondary forest areas surrounded by hilly areas, and estates such as oil palm estates and rubber plantations [11]. These environments increase the risk of spillover as the long tail macaques, *Anopheles* mosquitoes, and humans live in close interaction [11]. In Sabah, Malaysia, the breeding sites were also influenced by season. The rainy seasons from December to February and May to July provide temporary aquatic habitats for mosquito larva [10][12].

These mosquitoes are exophagic and tend to bite outdoors. The feeding behavior of *Anopheles* mosquitoes from the *Leucosphyrus* group peaks immediately after dark [10][12]. Chua et al. [12] stated that mosquito bites peak at around 18:00 to 22:00 h. Studies show that people are exposed to mosquito bites when they perform activities in the forest or return home from farms [10][11][12]. Recently, the *Umbrosus* group vector was found to bite humans earlier, around 07:00 to 11:00 h in Sarawak, Malaysia [13].

Studies have established that communities living on the edge of the forest, or performing forestry work, are at higher risk of developing a *P. knowlesi* infection [2][5][6][14][15][16]. Even travelers traveling to *P. knowlesi* affected regions are at risk to the *P. knowlesi* disease exposure [17]. Given the presence of asymptomatic *P. knowlesi* cases among household members and those not performing forest-related activities [2], there are gaps in the identification of other human activities or behaviors that put communities at risk.

Controlling zoonotic malaria is challenging, in part, due to uncertainty regarding vector distribution. To date, studies attempting to understand vector resting behavior have been unsuccessful due to difficulties in catching the vector in their natural habitats [10]. With the ongoing deforestation and changes in land use caused by anthropogenic activities, vector distributions are changing rapidly [10][12]. While significant attention has been given to vector behavior, to the researchers knowledge, no comprehensive review has been conducted on human behaviors that influence exposure to mosquito bites, causing *P. knowlesi* infection. Previous studies on human malaria have described various risk factors such as non-adherence to vector control tools [18][19][20][21], beliefs, and perceptions [22][23][24][25][26]. Despite extensive planning and intervention programs, the increasing incidence of *P. knowlesi* annually is a threat to public health [2][3]. Human behavior is a critical factor that should be explored and considered to improve malaria intervention [27]. The importance of tailored approaches to malaria varies across populations and contexts [27]. Acknowledging how human behavior plays a role in malaria exposure, including exploring the drivers and barriers, could guide towards more effective strategies of human-centered design approaches [27] and sustainable malaria intervention [28][29]. Therefore, understanding human behavior for *P. knowlesi* malaria is essential in view of its complexity due to the presence of its simian reservoir.

2. Human Behavior in Plasmodium knowlesi Malaria Infection

Human behavior is complex and is influenced by multiple factors. While sociodemographic, environment, and outdoor activities were commonly described as significant factors to *P. knowlesi* infection, the contextual factors involving the characteristics of human behavior can be further explored to improve future *P. knowlesi* malaria programs. the researchers study highlights the influence of psychosocial factors such as belief, attitude, perceived threat, lack of motivation, and self-efficacy on individuals' and communities' malaria preventive behaviors. Other contributing factors were due to community perspective toward the infection and healthcare system. the researchers argue that further exploratory studies should be performed in order to provide "logic" to the health outcome [30]. The understanding of human–vector contact patterns, and how they overlap in time and space, enables a more accurate representation of disease exposure [27][31]. Other factors such as social norms, perceived behavioral control, motivation to perform the behavior, and psychological factors such as attitude towards the

preventive behavior and emotions, can play a role in malaria exposure [32][33][34]. Social context and behavioral factors are among the known attributes of community perceptions and behavioral practices on antimalarial preventive measures [29]. Beliefs concerning *P. knowlesi* malaria etiology influenced their attitude, self-efficacy, and ways of coping with antimalarial measures [35]. A proportion of the community in Indonesia had local supernatural beliefs towards malaria [35], and this perception was also present among the Orang Asli community in neighboring country, Malaysia [36]. This signals a gap in disease prevention as communities have different perspectives and beliefs towards malaria. The practice of sorcery, rituals, and remedies are believed to protect them from evil spirits and ghosts [35][36]. In addition, the availability of healthcare services alone is insufficient to ensure good health practices if individuals' beliefs are unknown [35]. While most studies collected data by survey or questionnaire, analytical approaches should consider using exploratory study to detail the user perspective and experience in malaria exposure [27][29] to avoid participants responding to please the researcher [27]. Additional work is needed to address the remaining inquiries on human behavior and zoonotic malaria exposure.

The epidemiology of *P. knowlesi* infection is complex. While work and activities related to exposure play a role in malaria transmission in affected regions, other contributing factors, such as deforestation, disturbed the ecological balance of the area. As a result, these anthropogenic activities threaten the biodiversity and impact a higher risk of zoonotic malaria exposure as both monkeys and mosquitoes get closer to humans [2][6][11][12][35]. It is clear that *P. knowlesi* control is challenging, thus, individuals and communities need to culturally adapt to preventative measures, have sufficient knowledge about the issues, develop a positive attitude toward adopting health-supportive behaviors, gain support from and interact with others, and feel good about performing the behaviors [32][33][34]. Stakeholders must provide support to ensure a multi-collaborative effort in controlling this vector-borne disease [37], for example, by improving the housing structures, designing an innovative tool to avoid mosquito bites, and implementing the One Health approach [38].

Vulnerable communities living in rural and forested areas are at risk of *P. knowlesi* malaria. These communities have different norms and contexts that influence their living conditions. Malaria control strategies, especially those involving community education, should be tailored to fit each community depending on these factors [28][37]. Health promotion utilizing effective communication aids in preventive action should be considered, but such communication must be suited to the social context of the community [32][33][34]. A carefully designed malaria control program should consider the socio and behavior change (SBC) of the communities' beliefs, drivers, facilitators, and motivation towards malaria preventive behavior. For example, if the objective is to encourage the wearing of protective clothing, the communication objectives should consider the individual's emotions, social norms, and whether the tool is affordable [28]. Community-directed control programs may not be equally effective for all individuals in that community; however, and in this case, particularly competent individuals may act as advocates of SBC programs in the community [29][37]. Community participation in healthcare strategies should include all age groups to promote systematic, planned, and sustainable short- and long-term outcomes [37], as exposure to this zoonotic infection occurs in the young to elderly populations. Their participation can be facilitated by community dialogue and discussion of the social factors that may contribute to malaria exposure. This could provide collective opinions to help improve the social and structural environment, which in turn can be emphasized in malaria programs [29][37]. This method can help to provide community views to policymakers. Meanwhile, planning should

include the application of behavioral change theories to guide researchers and policymakers to develop health and other behavior changes in targeted communities [39].

Standard preventive measures such as insecticide residual spraying (IRS) and bed nets are ineffective against *Anopheles* mosquito bites because the vectors are mainly outdoor biters [27][28][29]. The current interventions may have relatively little impact in controlling the zoonotic malaria [10][11][12]. While the success of human malaria control and elimination has been contributed proportionally by the usage of vector control measures such as ITNs and LLINs there are gaps in the degree of personal protective measures in zoonotic malaria infection. The integration of the SBC by building the motivation of individuals, improving their belief, attitude, perceived threat, and self-efficacy in avoiding mosquito bites, and increasing the utilization of healthcare services, can facilitate individuals' protection against malaria [28]. Individuals' attitudes and motivations can influence family members and communities. By complementing the understanding of disease transmission more effectively, the characteristics of human behavior in exposure could be targeted in future studies [27][31][40]. While time can be an issue for acceptance and behavior changes, cues for action can be continuously performed to promote consistent preventive habits and behaviors [28]. In return, such bottom-up approaches can help to sustain malaria intervention programs [28][29][37]. This is pertinent because voracious mosquitoes are a nuisance only in the presence of humans around them, thus suggesting the need for research to consider this interrelationship [29].

A paradigm shift in *P. knowlesi* malaria control measures is required [11][12]; with consideration of the problem from multiple angles and a creative, bottom-up approach, involving the community in its planning, implementation, and evaluation [28][29][37]. Intervention programs should respect local priorities and needs; such as acknowledging local social, economic, and political circumstances [28][29], the researchers must look at the negligible but real risk among vulnerable communities, to fulfil the United Nations Sustainable Development Goals (SDG) to end the epidemics of infectious diseases and neglected tropical diseases, including malaria, by 2030 [41]. To achieve the SDGs, the interruption of malaria transmission requires the integration of community involvement using communication within the communities at risk, strong political commitment, and continuous disease surveillance [41]. Programs should strive for greater community participation to strengthen disease control, ensure sustainability, and foster transformative SBC approaches [27]. The Malaria Policy Advisory Group (MPAG) concluded that the emergent epidemiological changes of *P. knowlesi* requires extensive research and continuous surveillance [3].

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