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Authors

Githeko, AK
Ototo, EN
Guiyun, Yan

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Progress towards understanding the ecology and epidemiology of malaria in the western Kenya highlands: opportunities and challenges for control under climate change risk

AK Githeko[1], **EN Ototo**[1], and **Yan Guiyun**[2]

AK Githeko: githeko@yahoo.com; EN Ototo: ednaototo@gmail.com; Yan Guiyun: guiyuny@uci.edu

[1]Kenya Medical Research Institute, Centre for Global Health Research, Climate and Human Health Research Unit. P.O. Box 1578-40100 Kisumu, Kenya

[2]Program in Public Health, University of California, Irvine, CA 92697, USA

Abstract

Following severe malaria epidemics in the western Kenya highlands after the late 1980s it became imperative to undertake eco-epidemiological assessments of the disease and determine its drivers, spatial-temporal distribution and control strategies. Extensive research has indicated that the major biophysical drivers of the disease are climate change and variability, terrain, topography, hydrology and immunity. Vector distribution is focalized at valley bottoms and abundance is closely related with drainage efficiency, habitat availability, stability and productivity of the ecosystems. Early epidemic prediction models have been developed and they can be used to assess climate risks that warrant extra interventions with a lead time of 2–4 months. Targeted integrated vector management strategies can significantly reduce the cost on the indoor residual spraying by targeting the foci of transmission in transmission hotspots. Malaria control in the highlands has reduced vector population by 90%, infections by 50–90% in humans and in some cases transmission has been interrupted. Insecticide resistance is increasing and as transmission decreases so will immunity. Active surveillance will be required to monitor and contain emerging threats. More studies on eco-stratification of the disease, based on its major drivers, are required so that interventions are tailored for specific ecosystems. New and innovative control interventions such as house modification with a one-application strategy may reduce the threat from insecticide resistance and low compliance associated with the use of ITNs.

Keywords

Malaria; Highlands; Kenya; ecology; epidemiology; control

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Authors' contributions

All authors contributed to the review framework and concepts. They participated in the review of the literature and critical review and amendments of the manuscript.

Conflict of interest statement

1. Introduction

Malaria is a climate sensitive disease whose global, regional distribution and seasonality are closely linked to temperature, rainfall, humidity and socioeconomic development. Under the climate change regime, latitudinal and altitudinal shift of transmission suitability is expected (Lindsay et al., 1998; Tonnang et al., 2010). Warming of the East African highlands will create permissive conditions for transmission in areas that had very low seasonal transmission or where the disease was absent (Lindsay and Martens, 1998). This will further increase the burden of malaria in the region. Moreover the epidemics and severe form of the disease that have already been observed are likely to increase. It is therefore necessary to understand this emerging phenomenon so as to develop effective strategies for control and possibly eradication of the disease in the highlands.

Malaria epidemics were reported in the western Kenya highlands from 1928–40s (Matson, 1957) and then they disappeared until the late 1980s. However records indicate that low level transmission continued in the 1960–70s (Shanks et al., 2005). Severe epidemics occurred again in the late 1980s and continued until interventions were implemented and up-scaled in 2006. Historical temperature data indicates that there was above average warming across Africa from the early 1920s until mid 1940s and again starting from early 1980s to the current time (Hulme et al., 2001). Following the epidemics in the 1930s–40s malaria control was undertaken in the highlands of western Kenya using mass drug administration (Matson, 1957). In addition indoor residual spraying campaigns were undertaken in Nandi (1955–1957) and Kericho (1945–1949) districts in the highlands of western Kenya with DDT and dieldrin, respectively, and malaria was virtually eradicated (Roberts, 1964; White and Magayuka, 1972). However it seems that the climate prevailing during the control phase did not support malaria transmission. Indeed malaria disappeared in areas that were not sprayed. In the absence of serious malaria threats in the highlands after 1945 to about 1988 little or no research was carried out on the vector ecology and epidemiology of the disease in the highlands. Much of the research was focused in the lowlands of the Lake Victoria basin and the Kenya coast where malaria prevalence was holoendemic and mesoendemic respectively.

Historically the mean annual rainfall in the western Kenya highlands has been 1800–2000mm and the mean annual temperature has ranged from 17–20°C (Lalah et al., 2009; Stephens et al., 1992). The threshold mean annual temperature for malaria transmission is 18°C, below which transmission cannot take place.

The highlands are defined as areas at altitudes above 1,500m above sea level. Temperature is inversely related to altitude. Climate change has resulted in a gradual increase in the mean temperature while climate variability has lead to cyclic excursion of temperatures above and below the long term means (IPCC, 2001). These changes have a direct effect on the larval stage development, adult female blood feeding frequency and the rate of the sporogonic stage of the plasmodium development (Paaijmans et al., 2010). The global linear trend over the last 50 years has been 0.13°C per decade (IPCC, 2007). Unpublished data indicates that a warming temperature trend of 0.21°C has been observed in Kenya between 1960–2003 (http://country-profiles.geog.ox.ac.uk/UNDP_reports/Kenya/Kenya.lowres.report.pdf

Malaria epidemics in the late 1980 and early 1990s caused severe morbidity and mortality in the highlands leading to serious concerns within the health authorities on their causes. Towards the end of the 1990s systematic research was initiated to unravel the factors that were driving the epidemics. We review progress that has been made towards this effort and identify outcomes that lead to effective malaria transmission and epidemic control and also barriers that need to be addressed.

2. *Plasmodium falciparum* prevalence

Much of the early malaria data in the western Kenya highlands were based on hospital records (Hay et al., 2002; Shanks et al., 2000). However these records mainly reflect clinical cases (confirmed and unconfirmed) and they do not capture asymptomatic cases that may remain silent in the population.

Among the human population, parasite prevalence studies carried out before the interventions were implemented in 2006, it emerged that age, topography and drainage have a major impact on the level of transmission. The highlands were once considered as dominated by unstable transmission, however relatively high transmission has been found in certain ecosystems. In a poorly drained Yala river valley system the prevalence of *P. falciparum* infections at valley bottom was 68% and 26.7% at the hilltop among school children (Githeko et al., 2006). Prevalence rates ranging from 22.4–63.9% (Fillinger et al., 2009) were reported among school children in several study sites in the area. In terms of age distribution children from 1 to 4 years of age had the highest parasite prevalence (38.8%–62.8%) while in adults the prevalence declined to 2.9%–24.1% in the poorly drained Yala river ecosystem (Munyekenye et al., 2005). Asymptomatic malaria was frequent with episodes lasting between one month and 12 months. The long lasting episodes occurred at the valley bottoms, the major transmission hot spot (Baliraine et al., 2009) and these cases remain a significant reservoir of infections (Githeko et al., 1992). In the well drained ecosystems, such as the Fort Ternan the prevalence of *P. falciparum* in school children was 10%, this being 5–6-fold lower than in the poorly drained valley ecosystems (Koenraadt et al., 2006). Similar findings (13%) were reported in Kisii in an ecosystem that is characterized by good drainage (Guyatt et al., 2002; John et al., 2005). Assessment of immunological response in these ecosystems indicated differential exposure to infections. These findings indicate that malaria prevalence in the highlands range from hypoendemic-hyperendemic which translates to unstable and stable transmission. The eco-epidemiological systems have further been classified into epidemic and transmission hotspots (Wanjala et al., 2011). It has been observed in one study that the frequency of gametocytes increased from <1% to 5% just before an epidemic (John et al., 2005). In Burkina Faso the prevalence of gametocytes was significantly higher at the beginning of and during the wet season and the density was higher during the wet season than in the dry season (Ouédraogo et al., 2008). This phenomenon has been observed previously in the highlands of western Kenya and may explain the rapid evolution of malaria epidemics (Githeko unpublished)

3. *Plasmodium falciparum* genetics and immune response

Due to the dramatic effects of malaria epidemics in the western Kenya highlands, the disease has been referred to as "highland malaria" which is generally associated with severity and high mortality. There has been a need to determine whether the parasite populations in the highlands are different from those of the lowlands. Furthermore there was a need to determine whether the severity of the disease could be linked to the low level of immunity to *P. falciparum* infection. Frequencies of key mutations associated to sulfadoxine pyrimethamine resistance (dihydrofolate reductase (*pfdhfr*) and dihydropteroate synthetase (*pfdhps*) and chloroquine (chloroquine resistance transporter gene (*pfcrt*), and multi-drug resistance gene 1 (*pfmdr1*) were similar between the perennial transmission endemic lowlands and the highlands suggesting that the two populations were similar. Furthermore no differences were found in the gene mutation frequency between asymptomatic and symptomatic cases (Zhong et al., 2008). Analysis of 10 microsatellite markers from *P. falciparum* samples obtained from the highlands of western Kenya indicated high genetic diversity in the population and lack of any bottlenecks (Baliraine et al., 2010).

Severity of malaria in the highlands has been linked to lack of immunity. It has been shown that only 3.3% of individuals in a hypoendemic highland area had high levels of IgG to both circum sporozoite protein (CSP) and liver-stage antigen (LSA-1) of *P. falciparum*, compared to 43.3% of individuals in the hyperendemic transmission lowland area (Noland et al., 2008). Within the highlands a differential response to malaria using CSP and merozoite surface protein (MSP) has been demonstrated. Children living in poorly drained valley ecosystem had a 2-fold higher prevalence of these antibodies compared to those living in well drained valley and plateaus ecosystems (Wanjala et al., 2011). This phenomenon explains why malaria epidemics are frequent in ecosystems with a low frequency of immune response.

Currently malaria in the highlands has resulted in a substantial decline in transmission and this may result in impaired development of immunity which would increase vulnerability to severe disease if the control measures are not maintained. There is therefore need to monitor the immune response as malaria control continues.

4. Larval ecology

Anopheles gambiae s.l. and *Anopheles funestus* are the major vectors of malaria in the western Kenya highlands with *An. gambiae s.l.* comprising 90% of the adult population (Githeko et al., 2006). *Anopheles funestus* is associated with swamps and emergent vegetation and was more abundant during the dry seasons (Minakawa et al., 2005). Larval breeding habitats in the highlands are restricted to the valley bottoms (Munga et al., 2005) or to water bodies in hilltop plateaus in the highlands (Himeidan et al., 2009). The productivity of the habitats is affected by the quality of drainage, land cover and land use, stability of the habitats, temperature, predators and food availability. Larval habitat productivity determines the adult abundance and the rate of malaria transmission. Understanding larval ecology is critical to implementation of larval sources management using environmental interventions and bio-larvicides. Larval habitat stability is a function of topography and proximity to rivers, stream and other stable water bodies (Himeidan et al., 2009). Open drainage channels in reclaimed valley bottoms were the most stable breeding habitats though paddles are the most productive but the least stable *An. gambiae s.l.* larval habitats (Ndenga et al., 2011).

The quality of drainage and larval habitat availability are related. Valleys with slow moving rivers and a large flat bottom provide numerous stable breeding habitats while valleys with fast flowing rivers with a small flat surface have few stable breeding habitats. In ecosystems with poor drainage a mean monthly rainfall of 150 mm increases adult vector population (Githeko et al., 1996) however over 250 mm is required to increase adult population in the well drained ecosystems (Imbahale et al., 2011). In the poorly drained valley ecosystems rainfall increased the number of habitats 3-fold (Ndenga et al., 2011).

Larval development takes longer in the highlands compared to the lowlands; however the rate of development increased in reclaimed swamps which have higher water temperatures (Minakawa et al., 2006; Wamae et al., 2010). High larval mortality was attributed to low temperatures in some highlands sites (Koenraadt et al., 2003) and habitats such as natural swamps and forests (Minakawa et al., 2006). Larval mortality for *An. gambiae s.l* occurs at 14°C (Koenraadt et al., 2003)

The ecological framework of evaluating vector population dynamics in terms of larval habitat availability, stability and productivity has contributed significantly in understanding the spatial-temporal variation of malaria transmission in the highlands. These attributes have little variation in the hyperendemic lowlands. It has also greatly contributed in classifying the different ecosystems in terms on their transmission risks which has in turn lead to a new conceptual framework of integrated vector control.

5. Adult vector spatial-temporal dynamics and malaria transmission rates

Malaria vectors have clear temporal dynamics (Ndenga et al., 2006) and spatial distribution heterogeneity (Githeko et al., 2006). Within a valley ecosystem the majority of the adult females (*An. gambiae* s.l. 98% and *An. funestus* 99%) (Githeko et al., 2006), were found up to 500 meters from the breeding habitats which were clustered in the valley bottom (Zhou et al., 2007). Very few vectors are found at mid hill (1%) and at the hill top (1%). However during periods of exceptionally heavy rains the hill sides can become water saturated, resulting in springs that form stable breeding sites for *An. gambiae s.l.* In the well drained Marani river valley in Kisii district, the great majority of adult vectors were confined to the houses close to the valley bottom. However during events of prolonged heavy rains the numbers of houses previously devoid of vectors decreased markedly towards the hill tops (Ndenga et al., 2006). This condition is more likely to be observed during El Nino events when the warmer than normal temperatures and sunny interval are prevalent (Zhou et al., 2011).

Prior to ILLN interventions, poorly drained valleys had a 14.2–26.3-fold greater abundance of female vectors compared to the well drained valleys leading to different malaria transmission rates. While the poorly drained valley ecosystem had an entomological inoculation rate of 16.6 infectious bites per person per year (ib/p/yr) this was only 0.4 ib/p/yr in the well drained valley ecosystem (Ndenga et al., 2006). This is despite similar climate and weather (Wanjala et al., 2011). Earlier studies reported high transmission rates of 29.2 ib/p/year in *An. gambiae s.l* and 17.5 ib/p/year for *An. funestus* in the sugar cane growing ecosystem at 1,500 m asl (Shililu et al., 1998). The risk of malaria infection is highly correlated with topographical wetness index (Cohen et al., 2010).

Prior to 2002, no *An. arabiensis* was observed at altitudes above 1400–1500 meters above sea level (Minakawa et al., 2002; Shililu et al., 1998) but a very low proportion (0.8%) was observed in adult samples in 2003–2004 (Ndenga et al., 2006) and increased to 3% (Fillinger et al., 2009). A high proportion of indoor resting *An. arabiensis* (61.4%) has been reported at 2,056 meters above sea level (North Nandi District) in an area with moderate mean annual rainfall of 1,424 mm and mean annual temperature of 17°C (Kristan et al., 2008) and where both ILLN and IRS interventions have been undertaken (John et al., 2009). Higher proportions of *An. arabiensis* were reported in larval populations; 29.9% (Ndenga et al., 2011) and 33.7% (Kweka et al., 2011). Low adult survivorship and reproductive fitness have been proposed as barriers to the establishment of *An. arabiensis* in the western Kenya highlands (Afrane et al., 2007). These data suggest that *An. arabiensis* in the highlands may be highly exophilic and possibly zoophilic because although very few females have been collected indoors, a high proportion of the species has been identified in the larval populations. The increased use of insecticide impregnated nets in the highlands may be selectively reducing the proportion of *An. gambiae* to the advantage of *An. arabiensis* while events related to climate change may be increasing the environmental suitability for this species. *Anopheles arabiensis* is difficult to control due to its exophilic and zoophilic tendencies allowing it to survive chemical control better than the highly anthropophagic and endophilic *An. gambiae* and *An. funestus*.

6. Land use change and vector distribution

Human population growth has increased the demand for agricultural land and human settlement. The major land use changes that have occurred in the western Kenya highlands are deforestation and swamp reclamation. Both changes in land use types increase the suitability of larval breeding habitats by increasing their availability, water temperature and increasing photosynthesis and algae availability, a major larval nutrient. The survival of *An.*

gambiae s.l was 55–57% in deforested areas compared to 1–2% in forested areas and the breeding habitat water temperature was 3–4°C higher in the deforested areas (Tuno et al., 2005). Higher temperature and food availability decreased larval-to-adult development time and was associated with larger females (Munga et al., 2006). Restorations of swamps with Napier grass reduced water temperature by 2.8–4.7°C and *An. gambiae s.l.* larval population by 78.1–88% (Wamae et al., 2010). Deforestation in the highlands increased the larval-to-adult survivorship of *An. arabiensis* by 65–82%, and larval-to-adult development time was shortened by 8–9 days (Afrane et al., 2007).

These data suggest that informed land management such as swamp restoration and selective reforestation along major larval habitats has the potential for environmental management of malaria that would result in the reduced use of chemical control of vectors. Such an approach may increase the ecological goods and services in addition to malaria control.

7. Climate change and variability: effects on malaria transmission and the evolution of epidemics

The developmental rate of malaria vector larval stages (Bayoh and Lindsay, 2004) and blood feeding frequency of females are temperature dependent (Afrane et al., 2005; Rúa et al., 2005). In the western Kenya highlands changes have been observed in the monthly mean, maximum and minimum temperatures. For example the monthly mean, maximum and minimum all exhibited highly significant positive trends of 0.21°C, 0.24°C and 0.21 °C per decade, respectively as indicated by the Kericho meteorological station (Omumbo et al., 2011). The mean annual temperature for Kericho is 18°C and this is the threshold for malaria transmission. Besides a small increase in the average temperature, there have been frequent anomalous temperature excursions particularly in the maximum temperature (Githeko and Ndegwa, 2001). For example during the 1997/8 El Niño event, the maximum temperature in February 1998 was 5.9°C above normal (Kenya Department of Meteorology). It has been demonstrated that climate variability is strongly associated with the number of malaria outpatients in three western Kenyan highlands sites (Kericho, Kilgoris, and Eldoret), where climate variability contributed 40% of the temporal variance in malaria outpatient numbers, far more than the contributions from autoregression and seasonality (Zhou et al., 2004). There was an association between enhanced rainfall driven by the Indian Ocean Dipole positive mode and malaria cases in some sites in the highlands of western Kenya (Hashizume et al., 2009). However the El Nino Southern Oscillation is known to have a global impact and affects malaria hyper-transmission in South Asia, Africa and South America (Githeko and Ndegwa, 2001; Kovats et al., 2003).

Prolonged anomalous temperatures and unusually heavy rainfall are associated with El Niño events and malaria epidemics. There was a time lag of 1–2 months between the peak anomalous temperature and rainfall and a 1–2 month lag between rainfall and malaria epidemics. These observations were used to construct a weather based model for early malaria epidemic prediction (Githeko and Ndegwa, 2001). The model has a significant advantage over the clinical cases based early epidemic detection system that has a lead time of two weeks between the onset of the epidemic and its detection. Once the epidemic has started it can only be managed using effective drugs. In the case of early epidemic prediction, there is adequate time to launch vector control and reduce or prevent the epidemic. Blanket application of residual indoor spraying is not recommended for epidemic control due to cost and logistical considerations.

Until recently malaria transmission did not occur in the central Kenya highlands. However in the late 1990s sporadic reports of symptoms and malaria cases were reported. There was little evidence that there was local transmission because there were no records of malaria

vectors in the area. The first report of the malaria vector *An. arabiensis* appeared in 2006 (Chen et al., 2006). Thereafter analysis of temperature data indicated that before 1993 the annual mean temperature oscillated below and just above 18°C but thereafter there was a permanent shift to above this transmission threshold (Githeko, 2009). Data from the Kenya Demographic Health Survey 2008–09 (http://www.measuredhs.com/pubs/pdf/FR229/FR229.pdf) indicate that in <5 years old children in Central Province 6–7% of them were prescribed with artemisinin based therapy after developing fever. Data from the same region indicates a close association between increasing mean annual temperature and malaria cases (UNEP GEO-5 in preparation). Together with reported malaria cases in individuals who had no travel history (Epstein et al., 2011) and in an era of effective anti-malaria drugs, climate change was the only credible explanation for the spread of malaria to the Central Kenya highlands. There is a great need for epidemiological and entomological research in the Central Kenya highlands to clarify the prevalence of malaria and the distribution of the vectors in the area.

Until recently air temperature was used to estimate the potential for larval development in habitats in the highlands assuming that air and breeding habitat temperatures were similar. It has been shown that the mean water temperature in typical mosquito breeding sites is 4–6°C higher than the mean temperature of the adjacent air in typical larvae habitats, resulting in larval development rates, and hence population growth rates, that are much higher than predicted based on air temperature (Paaijmans et al., 2010).

8. Long term malaria infection and vector abundance surveillance

Among the factors that affect vector abundance and malaria transmission rates are climate change and variability, land use change and land cover change, vector control and change in species composition and dynamics. Malaria transmission can be affected by changes in vector insecticide susceptibility status. One of the pillars of Integrated vector management is monitoring vector populations and insecticide resistance.

The inter-annual variability of malaria in the highlands is strongly influenced by climate variability events such the El Niño. Most of the evidence for seasonal disease incidence is derived from passive case detection from health facilities while some evidence is available from active case surveillance from research activities. The passive case detection method is fraught with uncertainties due to clinical based diagnosis. Pediatric hospitalization data from 1999–2008 indicated a significant reduction of admissions after 2005 a period of up-scaled vector interventions and free treatment using artemisinin combination therapy (Okiro et al., 2009). After the up-scaled distribution of free ITNs in 2006, by the Kenya Government, that achieved a mean of 60% of the households owning the ITNs, vector densities (*An gambiae. s.l* and *An. funestus*) in the highlands declined by 90% (Zhou et al., 2011). A nine year (2002–2010) active malaria infection surveillance in two sites in the highlands demonstrated a dramatic fall on *P. falciparum* prevalence among school children. In a village located (Iguhu) in the poorly drained river Yala ecosystem, the monthly parasite prevalence dropped from an average of 33.8% (range from 18–57%) before July 2006 to 7.5% (range from 2–16%) between July 2006 and December 2008. In a well drained ecosystem, Marani in Kisii district, parasite prevalence declined from 10.1% before 2005, to 1.1% from 2005–2008 (Zhou et al., 2011).

A common resistance mechanism to DDT and pyrethroid insecticides is caused by an increase in the frequency of the knock down resistance (*kdr*) gene in the vector population. This gene is responsible for the detoxification of the pyrethroides and preventing the vector from being paralyzed and knocked down. By 2006, a conservative *kdr* allele frequency in *An. gambiae s.l.* was <1% in the highlands. However the monoxoogenase level of *An.*

gambiae from one of the highland sites (Iguhu, Kakamega) was significantly higher than the susceptible Kisumu strain of *An. gambiae* (Chen et al., 2008) indicating increased detoxification of pyrethroids by this vector. By 2009–2010 in a highland site in Kakamega the *kdr* L1014S allele was nearly fixed in the *An. gambiae* population, but was absent in *An. arabiensis*. Nevertheless declining populations of *An. gambiae* strongly suggest that the pyrethroid impregnated nets are still effective (Mathias et al., 2011).

9. Integrated vector management in the highlands of western Kenya

Integrated vector management has been defined as a rational decision-making process for the optimal use of resources for vector control (Beier et al., 2008). The current policy for vector control in Kenya includes the use of long lasting insecticide treated nets (LLN) and limited use of indoor residual spraying (IRS). The proportion of households with at least one ITN increased from 6% in 2003 to 54% in 2008 while the proportion of children under-five sleeping under an ITN the previous night increased from 5% in 2003 to 51% in 2008 (MOH Kenya). It has been found necessary to change the policy of targeting vulnerable groups and apply the universal coverage defined as one net for every two people.

The IRS application policy has been much less clear in part due to cost and logistical implications. Unlike in the lowlands where vector breeding habitats are ubiquitous, they tend to be confined to valley bottoms along rivers and streams in the highlands (Minakawa et al., 2005) leading to 98% the adult female vector population being confined to the valley bottoms (Githeko et al., 2006; Zhou et al., 2007). This type of distribution allows targeted vector control. Results obtained from a trial targeting IRS (Lambda-cyhalothrin ICON) in houses where 95% of the vectors were found, reduced *Anopheles gambiae* densities by 96.8% at the target and 51.6% in the adjacent non-targeted area while *Anopheles funestus* densities were reduced by 85.3% and 69.2% in the target and non-target area respectively. This strategy led to a 64.4% reduction in malaria prevalence in the target area and by 46.3% in the non-target area (Zhou et al., 2010). Thus by targeting about 25% of the houses with IRS a significant reduction in disease transmission was achieved as opposed to blanket coverage of the entire area.

Within the LLN program further reduction in transmission can be achieved in the highlands by targeting larval stages of the vectors at the valley bottoms. Bio-larvicides Bti and BS were targeted at larval breeding habitats in an area with a 40% ITN coverage and reduced the entomological inoculation rates by 73% compared to the non-intervention sites. The use of ITNs alone reduced malaria incidence by 31% and this was further reduced to 51% by larviciding (Fillinger et al., 2009).

While this strategy has achieved a significant reduction in malaria transmission, the frequency of larvicide application presents a major challenge. Studies are required to determine the best options for targeting the larvicides in time and space.

Integrated vector control management requires intensive data input as a bases and rationale for decision making. The epidemiology of malaria in the highlands has greater variance than in the lowlands and it is also changing due to the impact of changing climate, land use change and intervention. Continued monitoring and surveillance is required so as to respond appropriately.

10. Early epidemic prediction and control options

Significant progress has been made towards understanding the evolution of malaria epidemics in the western Kenya highlands. It has been shown that the malaria epidemics are associated with temperature and rainfall anomalies (Githeko and Ndegwa, 2001). Further

research on early epidemic prediction models has been completed in the highlands of East Africa (Kenya, Tanzania and Uganda) resulting in ecosystem-specific models and their high positive predictive power, sensitivity and specificity has been documented (Githeko Unpublished data). These models will be integrated into climate risk management within the malaria control programs in East Africa. Analysis of malaria cases and climate in seven sites in the East African highlands indicated high spatial variability in the number of cases (Zhou et al., 2004). Heterogeneity in vector and malaria infection prevalence has been associated with topography (Brooker et al., 2004; Githeko et al., 2006) and vectors are clustered at valley bottoms (Minakawa et al., 2005; Minakawa et al., 2006; Zhou et al., 2007). The rate of malaria transmission has been associated with drainage characteristics (Ndenga et al., 2006) and subsequently the immune response level. There was an 8.5- fold and a 2-fold greater parasite and antibody prevalence respectively, in the poorly drained U-shaped compared to the well drained V-shaped valleys. (Wanjala et al., 2011). Moreover the poorly drained valleys had a 3-fold greater abundance of *An. gambiae s.l* vectors than the well drained valleys (Ototo et al., 2011). While climate variability has a temporal effect on the evolution of the epidemics, terrain, topography and hydrology affect the spatial variability and sensitivity of an area to severity and extent of an epidemic.

Analysis of malaria prevalence in the western Kenya highlands in relationship to defined ecosystems (Wanjala et al., 2011) indicated that the disease occurred in low frequency in the well drained ecosystems where transmission is very weak due to low vector density (Ndenga et al., 2006). There is evidence from long-term monitoring that in such ecosystems LLNs alone have significantly reduced malaria transmission from 10% to 1% (Zhou et al., 2010). This raises the question whether IRS is justified in such an eco-epidemiological setting. Nevertheless climate variability may increase the risk of transmission significantly and this may require targeted IRS interventions. The early epidemic prediction models are decision assessment tools which can be used to quantify the climate risk and determine if the risk warrants extra interventions. Thus integrating the climate based early epidemic prediction tool can reduce the uncertainly in decision making and in addition potentially reduce vector control that may not be cost effective.

11. Conclusion

Prior to the 1980s the ecology and epidemiology of malaria in the western Kenya highlands was not well known. Through modeling it became clear that climate change and variability could increase malaria transmission and explain the occurrence of the epidemics (Pascual et al., 2006). It has been suggested that climate change and drug resistance can interact through increased transmission and the two phenomenon may not be mutually exclusive (Artzy-Randrup et al., 2010). Topography, terrain characteristics and hydrology have been shown to explain the spatial variability in malaria prevalence, and sensitivity of some areas to epidemics. The same factors can explain the contrasting immune response in the human population. The development of the climate based early epidemic prediction models has considerably increased the possibility of epidemic prevention instead of epidemic control. Vector ecology indicates that transmission is focal thus providing opportunities for targeted interventions. Evidence is emerging that the different eco-epidemiological systems will need interventions based on their levels of transmission. While LLNs will be sufficient to control malaria in the low transmission ecosystems which are also epidemic hotspots, supplemental targeted IRS will be required in the moderate to high transmission ecosystems. Within the integrated vector management (IVM) strategy the environmental interventions such as swamp restoration provide a sustainable non-chemical approach to malaria control. Studies are required to determine the efficacy of modified houses as a novel malaria control strategy in the highlands (Atieli et al., 2009).

Monitoring vector population dynamics, species redistribution, feeding and resting behavior, resistance to insecticides and climate risks will inform the integrated vector management and malaria control. There is emerging evidence that sustained IVM could interrupt malaria transmission in the highlands (John et al., 2009) and leading to possible eradication.

Further research is required to clearly map distinct ecosystems as defined by terrain, topography and hydrology as this is required in developing ecosystem based IVM interventions.

Research Highlights

- Topography and hydrology explain malaria spatial variability and immune response

- Transmission is focal thus providing opportunities for targeted interventions

- Climate based early epidemic prediction models facilitate epidemic prevention

- Monitoring entomological parameters inform integrated vector management

- Interventions should be based on ecosystem-specific transmission parameters

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