International Scholars Journals

African Journal of Malaria and Tropical Diseases ISSN 4123-0981 Vol. 2 (8), pp. 066-073, August, 2014. Available online at www.internationalscholarsjournals.org © International Scholars Journals

Full Length Research Paper

A study of the use of targeted indoor residual spraying (IRS) as a single malaria intervention in the western highlands, Kenya

***[1]Jomo T. William, Moi Musyoka[1], Mwai I. Uhuru[2] and Josephat E. Musalia[2]**

[1]Egerton University of Science and Technology, Department of Biological Sciences, Njoro, Kenya.
[2]Daystar University, Department of Biological Sciences, Nairobi, Kenya.

Accepted 17 July, 2014

The study investigated the use of targeted indoor residual spraying (IRS) as a single malaria intervention in the western highlands, Kenya. Houses were randomly selected in study sites and IRS targeted 30% of houses at focal sites 'hotspots' at valley bottoms. Indoor resting densities of adult *Anopheles gambiae s.s* were monitored biweekly by pyrethrum spray capture in sprayed and control houses. Microscopic examination of blood smears were used to confirm malaria infection and records on malaria cases from health centers were analyzed and used to determine changes in malaria prevalence. The indoor *A. gambiae s.s* declined after IRS. Low vector densities were also recorded in the control houses with no malaria cases. Malaria cases reported at health centers dramatically declined after the targeted IRS. Low coverage targeted IRS was effective as a single intervention strategy as it led to decline in annual disease prevalence from 12 to 1% in the study sites. The effectiveness of targeted IRS appeared to be dependent on anthropophily of the local vector, its susceptibility to the insecticide and seasonal nature of malaria transmission.

Key words: Malaria prevalence, IRS, malaria vector.

INTRODUCTION

Malaria transmission patterns in Kenya are classified based on transmission intensity (Snow et al., 1998 a. b; Otsyula, 2002). These are endemic and unstable endemic zones and epidemic zones. The endemic zones primarily exist in lowland areas (<1400 m) and experience high intensities of transmission which is usually continuous throughout the year. Individuals in these zones acquire some degree of immunity through continued exposure to infective mosquito bites. The unstable endemic malaria zones however, experience moderate intensities of transmission with seasonal and year to year fluctuations (WHO, 1999). The epidemic zones located in highland areas (>1500 m) experience irregular rapid increases in malaria incidences usually related to seasons and population movements (Otsyula, 2002). Most populations in the epidemic zones are non-immune and therefore, all age-groups are at risk of severe malaria infection and death in the absence of appropriate intervention (WHO, 1999; John et al., 2004).

The western Kenya highlands are considered as malaria epidemic-prone areas with seasonal out-breaks (Some, 1994; Malakooti et al., 1998; Guyatt et al., 2002). The forecast for the future is not favorable as more seasonal malaria epidemics are more likely to be frequent and intensify in future (McMichael and Githeko, 2001). Approaches to control previous seasonal malaria epidemics in the Kenya highlands involved a combination of mass diagnosis and administration of anti-malarial drugs complemented with extensive and several rounds of indoor residual spraying (IRS) covering at least 80% of human dwellings (Strangeways-Dixon, 1950; Roberts,

*Corresponding author. E-mail: moiwilliam101@gmail.com

1964) and insecticide treated nest (ITNs) (ARC, 2002). The collective implementation of these interventions was cumbersome, costly and required massive logistical effort, with numerous obstacles in their implementation and was disliked by communities (WHO, 2006). In addition, each of the interventions has inherent limitations depending on logistics, where applied and the disease transmission pattern.

There has been an urgent need for re-evaluation of current technology and its appropriate application to achieve maximum results. In this regard, the potential for modified application of one of the malaria control strategies for effective disease control and prevention needed to be explored. Nowhere else was this more relevant than in the western Kenya highlands where highly variable levels of malaria combined with low levels of functional immunity produce devastating seasonal malaria epidemics with high mortality rates in all age-groups (TDR, 1998). Scarce resources should be applied where it will have the greatest impact on the disease and therefore, be more acceptable to the affected community.

Studies in the western highlands of Kenya indicate that, the malaria transmission pattern is highly seasonal (Lindsay and Martens, 1998), focal in nature (Kacey et al., 2006) and perpetuated by a monomorphic vectorial system of endophilic *Anopheles gambiae s.s* (Mulambalah, 2009). We hypothesized that, appropriate targeting of IRS to the focal points (hot spots) before the transmission season would be an effective single control/ preventive measure as opposed to a combination of intervention strategies. The purpose of the study was to assess the effect of targeted low coverage IRS using *lambda-cyhalothrin* (trade name ICON) on indoor malaria vector densities, malaria prevalence in study sites and to propose IRS for consideration as the sole intervention measure in specific highland areas of Kenya.

MATERIALS AND METHODS

Study sites

The study was conducted in North Nandi District (0°21'52"N and 0°16' 56" N in longitude and 35°5'20"E and 34°59'7"E in latitude), in the highland area of Kipsamoite (2001 population approx. 3400 individuals) and Kapsisiywa (2001 population approx. 3000 individuals). The study sites were selected because they were located 1500 m above sea level, an altitude defined as characterizing the highland area and malaria epidemics and outbreaks had been reported within the sites previously. Also, two government health centers present within the sites were considered important in carrying out prevalence studies because they served large and varying catchment populations and were accessible. The Government of Kenya health centers (Kapsisiywa and Kipsamoite health centers) were the only health facilities within the study sites.

The topography of the study sites comprises hills, valleys and plateaus. Rivers and streams run along the valley bottoms in the valley ecosystem and swamps are a common feature. The study area has two rainy seasons, long rains season, from March to May, referred to 'long rains' on the account of duration and high amount of rainfall received in many parts of the highland. The second season is the short rains from the months of October to December, during which period, the area experiences depressed rainfall that is also poorly distributed both in space and time (Figure 1). There are variations in temperature; the warmest temperatures are experienced in March and the coldest in July with the mean monthly temperatures ranging from 17 to 19°C. The two study sites were about 20 km apart with households located from 1900 to 2000 m on the hillsides at different elevations.

The study sites experience unstable, sporadic malaria transmission. A peak in transmission often follows the long rains from March to May but sometimes may extend up to July. Mosquito surveys indicated that, the predominant indoor resting vector is *A. gambiae s.s.* (97.5%) with *Anopheles funestus* (2.5%) (Kacey et al., 2006), as a minor vector.

Targeted low coverage IRS

In collaboration with the Division of Vector Born Diseases (DVBD) in the Ministry of Health, Kenya, houses within 150 m from valley bottoms were considered as high risk areas (hot spots) and were counted and coded. A random sample of 90 houses out of a total of 300 (30% house coverage), was used for targeted IRS in each study site and a similar number of houses from the same high risk areas used as unsprayed controls.

Indoor residual insecticide spraying was carried out in the sites from March to April 2007 in targeted houses whose occupants consented to spraying. The spraying technique involved the use of pressure pumps fitted with nozzles to deliver the insecticide, lambda-cyhalothrin (ICON) at the recommended dosage of 0.02 to 0.03 mg/m^2. With the spray lance kept at 45 cm away from the wall surface, spraying was done from roof to the floor using a downward motion with a spray discharge rate of 740 to 860 ml per minute. The house owners were advised not to re-plaster or re-paint the sprayed surfaces. To evaluate the efficacy of targeted low coverage IRS, changes in indoor adult malaria vector densities in sprayed and unsprayed houses were evaluated and malaria prevalence in the study sites were also used as indicators of success.

In-door vector sampling

Indoor vector sampling was carried out in both sprayed and unsprayed houses by the pyrethrum space spray method (WHO, 1975). Total indoor resting mosquitoes were collected from randomly selected houses in the study sites. The vector collections were carried out fortnightly in each cluster area from 06.00 to 08.30 am. The sampling was done before and after indoor residual spraying for periods covering the dry and rainy seasons. All the knocked down vectors were collected and transported to the Kenya Medical Research Institute (KEMRI) laboratories for identification by morphological features and polymerase chain reaction (PCR) and natural infectivity by sporozoite (Mulambalah et al., unpublished data). Malaria vector densities were determined by enumerating vector species numbers per house and dividing the total by the number of houses. The average number of adult female *Anopheles* of a defined species determined the *Anopheles* density or vector density. It is expressed as a relative proportion per house per month (Bruce-Chwatt, 1985).

Surveillance for clinical malaria and subject recruitment

The Kipsamoite and Kapsisiywa Health centers, Kenyan Ministry of health clinics were the only health care facilities in the study sites and were situated one in each study site, respectively. For logistical reasons and a poor communication network, these health centers were the only sampling points used during the study. Previous

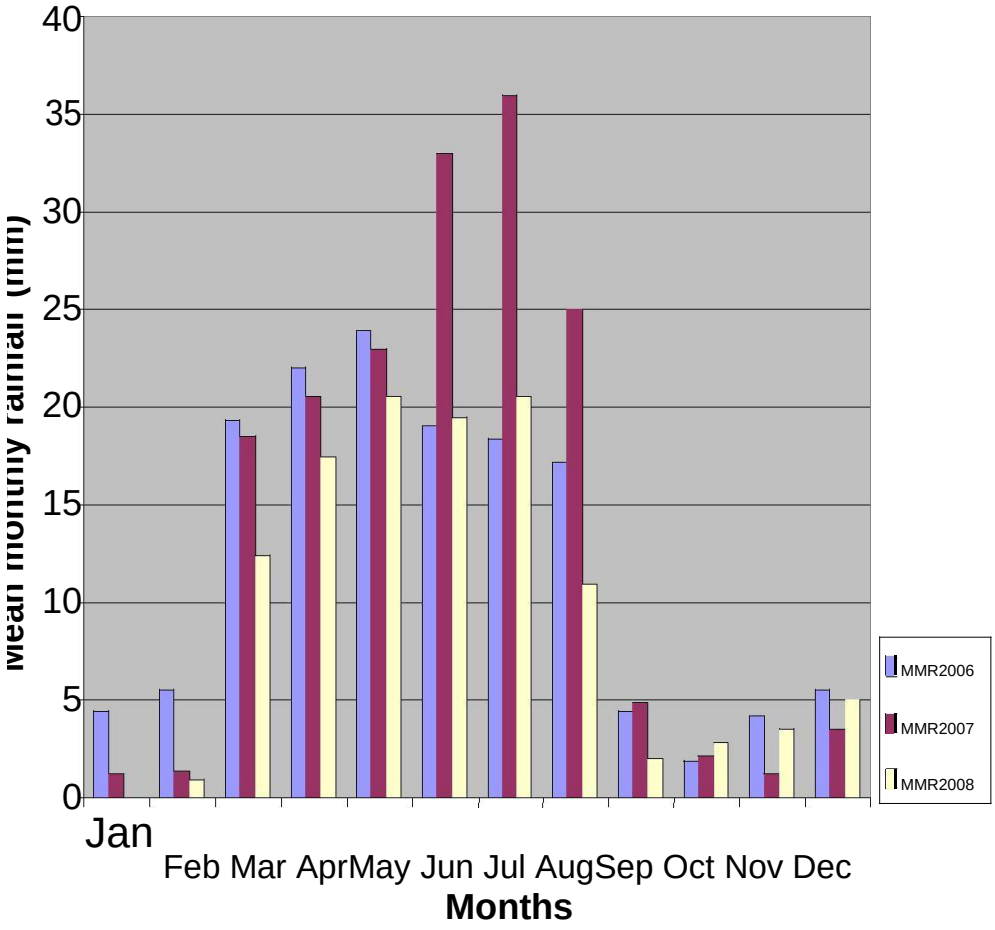

Figure 1. Mean monthly rainfall at Kipsamoite and Kapsisiywa 2006 to 2008. MMR2006, mean monthly rainfall 2006; MMR2007, mean monthly rainfall 2007; MMR2008, mean monthly rainfall 2008. Data source: KEMRI data unit.

population studies indicated that >80% of the population in the sites sought care at these centers when they had symptoms of malaria. Participant recruitment was based on individuals presenting at health centers. Participant sampling from the study population was obtained by sampling a consecutive series of participants attending clinic until sample size was obtained or the nearest figure to sample size was obtained. Sampling was carried out at 2 week intervals during the study period. Eligibility was open to consenting individuals of all ages who lived in the study sites for more than 6 months of the year or if they were new to the area, who planned to live in the area for more than 6 to 12 months of the year

A malaria case was defined as an individual from the study sites who presented to the health centre with symptoms of malaria (fever, chills, severe malaise and headache, vomiting for children) and presence of *Plasmodium* parasites on microscopy testing of his/her blood smear. All other individuals residing in Kipsamoite and Kapsisiywa, including those not reporting to the health clinics and those with slide-negative results, were considered non-diseased controls.

The sample sizes, from each study site, with a 95% confidence interval and precision level of 5% were arrived at using the formula:

$$n = \frac{z^2 (pq)}{d^2}$$

In this equation, n is the sample size, z is the critical value of the standard normal distribution at the 5% level (1.96), p is the malaria prevalence estimate, q = 1- q and d is the precision level at 0.05. This translated into a sample size of 1360 individuals from Kipsamoite and 1200 from Kapsisiywa.

Blood collection and processing

Ethical approval for the study was obtained from the KEMRI National Ethical Review Committee. Written informed consent for study participation was obtained from all consenting individuals. A blood sample 0.5 to 1.0 ml was obtained by the following procedure at two health centers; preparation of site (finger) with alcohol, pricking of the fingertip with a lancet and obtaining the blood sample on a clean 25 x 75 mm slide in a 10 to 30 s period. The blood was spread out to make thick/thin films/smears, dried and fixed in methanol and stained in 4% Giemsa for 30 min. All stained blood films were examined microscopically at1000× objective under oil immersion to identify the malaria parasite species. Microscopic examination was done at the health centers and the presence of malaria parasite species in sexual or asexual stages was considered a positive diagnosis. A second and third blood examination was done at KEMRI for quality assurance. The whole slide was carefully scanned before being declared negative. Slides were reported negative for parasites only after examining at least

50 fields. The following relevant parameters were also collected from each subject including age, residence; prior use of any anti-malarial measures for instance drugs, as well as insecticide-treated nets (ITNs).

Data analysis

Anopheles vector indoor densities

Anopheles mosquito densities were calculated by determining the actual numbers of females of each species per house. The actual number was increased by 15% to compensate for 5% of female that fly out-doors after feeding (Gilles, 1954) and to allow for 10% loses during spray catching (WHO, 1963). The mean house densities were calculated and then expressed as geometric means. The equation used is given below:

$$\log (\text{mean} +1) = \sum \frac{\log (n+1)}{N}$$

Where, n_1, n_2……. represent actual values of individual catches and N represented total number of all catches (Haddow, 1960). Further, the mean percentages of the total catch was calculated and used to illustrate monthly variation in the study sites/ sprayed/ unsprayed houses. The analysis of variance (ANOVA) was used to determine any variations in vector densities between sprayed and unsprayed houses and the effect of spraying on the vector densities in the two study sites.

Malaria prevalence

Study site malaria prevalence and age group related malaria prevalence was determined as described by Prybyski et al. (1999). Annual malaria prevalence in study sites was calculated as described by (Simon et al., 2002) where all malaria cases in each study site were divided by the population of each site and multiplied by $10^{n.}$ The base population was defined as individuals residing in study areas on 1st July of each year.

RESULTS

Indoor *Anopheles* collections and density estimation

Only *A. gambiae s.s* was collected in appreciable numbers. The other known malaria vectors, *A. funestus* and *A. arabiensis* were rarely collected, one specimen of each of the two species were collected during the study period, these were statistically inadequate to work out monthly densities in order to calculate a meaningful trend. The densities of *A. gambiae s.s* collected from sprayed and unsprayed houses from the study sites are indicated in Figure 2.

The in-door spraying had a significant influence on the indoor vector densities as indicated by the significant difference in *A. gambiae s.s* vectors collected from sprayed versus unsprayed houses (ANOVA, P = 0.005). However, a comparative analysis indicated that there was no significant difference (ANOVA, P = 0.588) in vector densities in sprayed houses between the two study sites. This suggested that, IRS had the same effect in both study sites. Ideally this means that, IRS led to a decline in vectors in both sites and that IRS had a uniform effect on vector densities in the two sites. The monthly density of *A. gambiae s.s* in unsprayed houses followed the seasonal trend (Figure 2), peaking during the long rainy season and declining during the short rains and dry seasons. A significant difference in seasonal densities was determined (P = 0.005).

Malaria prevalence

Malaria in the Kenyan highlands in general is unpredictable and sporadic. The only prevalence figures that were available for reference on previous malaria prevalence were collected in 2006 when there were no control measures and in 2007 when targeted low coverage IRS was used in the study sites. The monthly malaria prevalence in the presence and absence of the control strategy was calculated. The comparative monthly prevalence figures for 2006 and 2007 are shown in Figure 3. In the absence of any control strategy, malaria prevalence in the study sites generally followed the same pattern in 2006. Cases of malaria increased during the month of March through April and May (KAP2006 and KIP2006). Peak transmission was recorded at mid-year during the months of June to July and thereafter, a decrease from August. No cases of malaria were recorded during the last three months of the year (October to December, 2006; 2007). There was no significant difference in malaria prevalence in the two study sites (ANOVA, P = 0.213) in 2006.

The targeted spraying in the study sites virtually controlled malaria (KAP2007 and KIP2007). This intervention strategy resulted in a decline of annual malaria prevalence from 12% in 2006 to 1.1% in 2007 in Kipsamoite and from 10% in 2006 to 0.6% in 2007 in Kapasisiywa. All adult female participants admitted to using or having used ITNs specifically for their infants as advised at ante-natal clinics. This was reflected by an absence of malaria positive cases in age groups <1 year in both study sites (Figure 4). Malaria positive cases were recorded in all other age groups though no significant variation was determined amongst the age groups (ANOVA, P = 0.681) confirming that all other age groups had the same risk of malaria infection.

DISCUSSION AND CONCLUSIONS

Malaria disease focal points or the ‘hot spots’ is new phenomenon in highland areas of Kenya. These are areas with the highest concentration of malaria vectors and highest parasite prevalence in the local population (Kacey et al., 2006). Focal points act as ‘reservoir of infection’ because of the availability of numerous breeding sites in the form of shallow streams/rivers, stagnant pools,

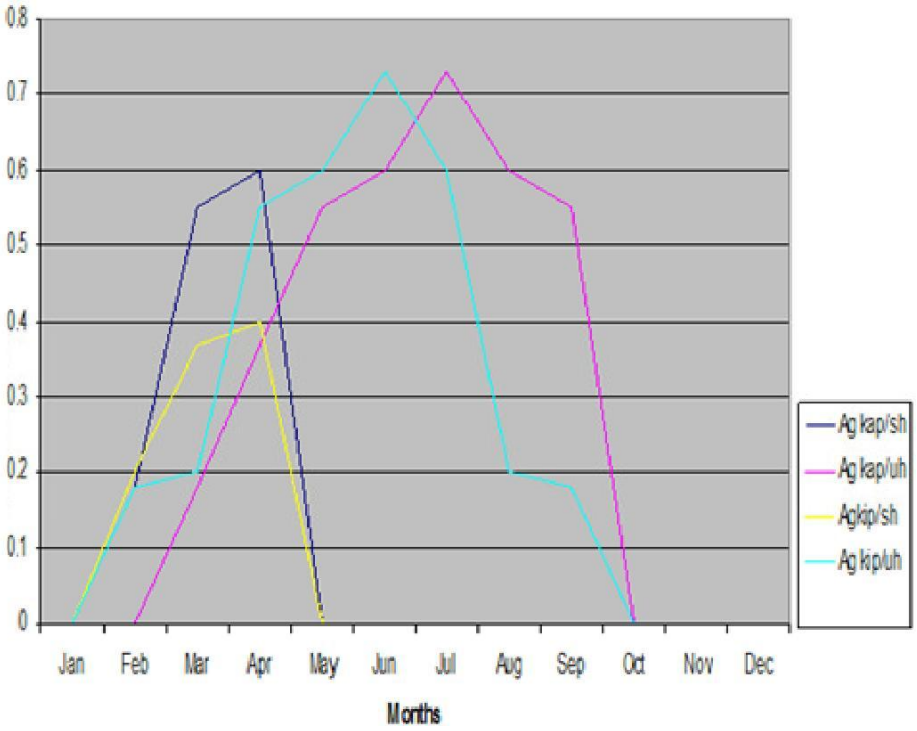

Figure 2. *A. gambiae* s.s monthly density distribution in sprayed and unsprayed houses in 2007. Ag kap/sh, *A. gambiae s.s* densities in sprayed houses at Kapsisiywa site; Ag kap/uh, *A. gambiae s.s* densities in unsprayed houses at Kapsisiywa site; Ag kip/sh, *A. gambiae* s.s densities in sprayed houses at Kipsamoite site; Ag kip/uh, *A. gambiae* s.s densities in unsprayed houses at Kipsamoite site.

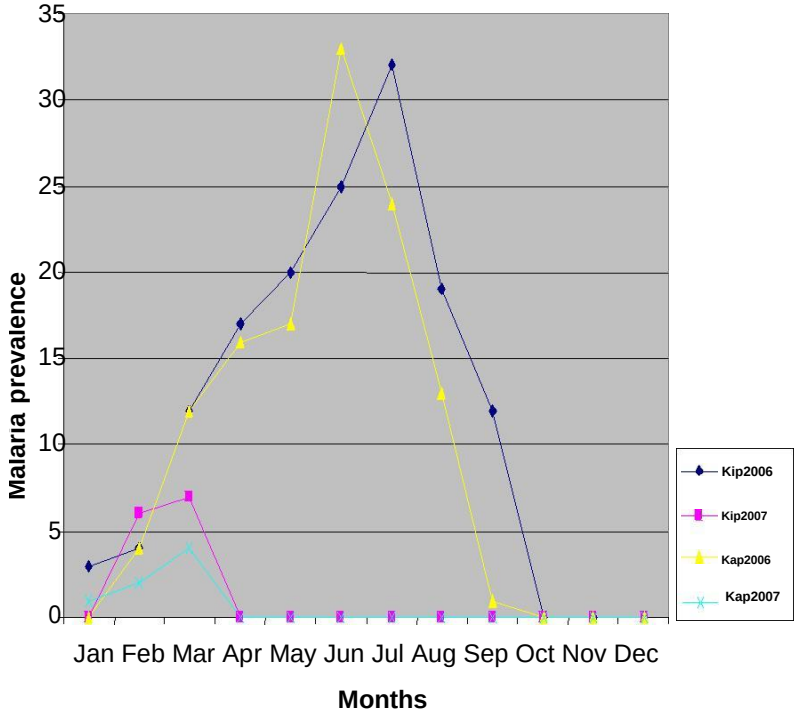

Figure 3. Comparative Monthly malaria prevalence in Kapsisiywa and Kipsamoite 2006 and 2007. Kip2006, Kipsamoite in 2006; Kip2007, Kipsamoite in 2007; Kap2006, Kapsisiywa in 2006; Kap2007, Kapsisiywa in 2007.

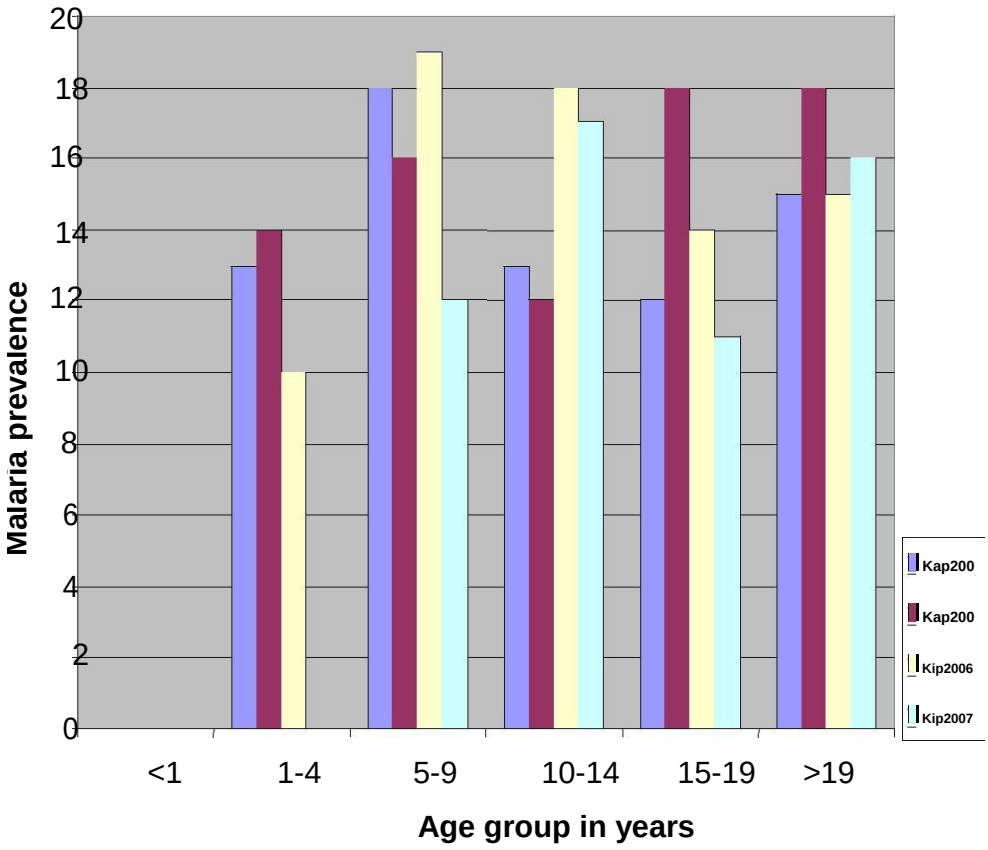

Figure 4. Age group malaria prevalence. Kap2006, Kapsisiywa in 2006; Kap2007, Kapsisiywa in 2007; Kip2006, Kipsamoite in 2006; Kip2007, Kipsamoite in 2007.

swamps and irrigation canals at valley bottoms. With a large population settled within close range of breeding sites, close contact with vectors is easily established and therefore, there is an increased chance of disease establishment and spread to the nearby human hosts and further to surrounding areas within and outside the study sites through population movements. This is possible when changes occur in the number of persons carrying infective gametocytes who initiate malaria transmission and consequently, epidemics through increased mosquito transmission (Shanks et al., 2005b). Infected malaria vector active and passive dispersal possibly play an important role in spreading disease beyond the 'hot spots'. It is for these reasons that focal points are considered favorable and important targets for malaria intervention in both epidemic and non-epidemic periods (Githeko et al., 2006)..

To transmit malaria within and outside a focal point, the malaria vector must ingest infectious gametocyte forms of the malaria parasite from an infected person, survive long enough for these to successfully transform into infectious sporozoites and then, bite another susceptible human host. For *Plasmodium falciparum*, the most prevalent parasite species in the present study sites (and in Africa) and the most dangerous, this process takes a minimum of 10 days (Beier, 1998). Malaria intervention strategies that target this disease transmission process include ITNs and IRS.

Malaria transmission in study sites mainly occurred from the onset of long rains in March to the onset of cool weather in July to August with peak transmission in mid-year (June to July). This is explained by the fact that, the ambient temperature and rainfall are suitable during the period for vector build up and parasite sporogonic development rates increases and thus, *Anopheles* vectorial capacity increases rapidly (MacDonald, 1957). It was therefore appropriate to target malaria intervention strategies just before the onset of the season.

The study results indicate that, the transmission process was completely halted in age group < 1 year in which no positive cases were detected. It is suggested that, this group of subjects were exposed to anti-malarial drugs and/or slept under treated nets given free during visits to ante-natal clinics by expectant mothers. Insecticide treated bed nets are issued free by the Ministry Health and NGOs to expectant mothers in malarious areas, who are also strongly advised to sleep under the nets and extend the same to their new-born. Indeed, ITNs provide appreciable protection against malaria infection (Bermejo and Veeken, 1992; Thomson, 1996) but our

but our finding suggest that, protection is biased/ selective towards infants and was not beneficial to the wider community in terms of malaria prevalence. Possibly, mothers cover infants under treated nets excluding other household members. It is also possible that, communities are not properly advised on the protective effect of nets both for infants and adults considering that malaria occurrence is unpredictable and sporadic in the study sites.

The application of low coverage targeted IRS led to a significant decline in malaria indoor vector density and in annual prevalence in study sites. This was attributed to the presence of insecticide residues on the walls. The insecticide may function as non- contact repellent thus, preventing anthropophilic *A. gambiae s.s* entry into human habitations. Also, if the vector entered the house in-spite of the repellent action, a contact irritant action on the anopheles vector may cause it to exit before settling on the sprayed walls. If the contact irritant action failed then, contact toxicity of the insecticide could result in mosquito death after direct contact with treated wall surfaces. The three attributes of ICON (repellent, irritant and toxicity) and possibly induced exophily make it ideal and effective in preventing human-malaria vector contact, an essential link for malaria establishment and spread in a community. This is a possible explanation of the decline of both indoor malaria vector densities and malaria prevalence during a period when malaria transmission would have otherwise peaked. These findings are similar to related studies that have confirmed that IRS can cause a dramatic decline of disease transmission within communities (Molineaux and Gramiccia, 1980; Romi et al., 2002). By targeting the source of the infection, the 'hot spots', IRS appears to stop the transmission process at the initiation stage and because the insecticide persists on treated surfaces, it continues to suppress disease establishment at the 'hot spots' and prevents its spread to the wider community.

The concentration of the 'hot spots' at valley bottoms is most likely due to low altitude, warmer temperatures, higher numbers of human hosts and proximity to breeding habitats favorable for *Anopheles* survival. The warmer temperatures at low-lying areas also favor faster development of *P. falciparum* within the vector. At higher altitudes (hilltops), the associated decreased temperature may be a limiting factor in malaria vector populations and malaria parasite development and therefore, exclusion of 'hot spots' in higher areas in study sites. In addition, the hill slope from low-lying land to hilltop cannot allow formation of pools of water necessary as vector breeding sites. Low air temperatures during July to August in the Kenya highlands is known to shorten adult stage longevity of *A. gambiae* species and inhibit *Plasmodium* sporogonic development (Minakawa et al., 2006) which could drastically reduce malaria vector populations and limit the transmission process therefore, complementing the targeted IRS approach.

Without data for multiple years, it is difficult to discern if the 'hot spots' are transient affected by weather and human/land use factors or if they relate to more long-standing foci of infection that may affect a larger area beyond the study sites (Kacey et al., 2006). The presence of malaria vectors in highlands does not always result in malaria transmission. Transmission in highlands is known to be negatively affected by low vector infective bites (Shililu et al., 1996) hence, low infection rates. Prevailing low temperatures at high altitude areas affect both vector and parasite development negatively (Shanks et al., 2005a). This explains the presence of vectors in control houses but no significant malaria cases detected. However, the recognition of consistent malaria disease foci with abundant vector numbers or cases of malaria permit control efforts to be directed at specific geographical areas thus, reducing costs and increasing effectiveness. Control of transmission in such 'hot spots' eventually seems to lead to elimination of cases in 'çool spots' and this has an overall beneficial effect on a wider area than the original targeted zones. Indoor residual spraying is one of the most effective anti-malarial strategies for obtaining a rapid large scale impact at affordable cost (Najera and Zaim, 2001). Malaria control and prevention by killing adult mosquitoes in targeted houses is favored (Carter et al., 2000; Killeen et al., 2000; Walker, 2002). A study carried on the use of IRS and ITNs, Guyatt et al. (2002) found that, IRS was both more effective and cheaper than ITNs when applied in communities subjected to low, seasonal risks of infection similar to the situation in the present study sites.

Indoor residual spraying as a single intervention strategy in malaria control in the highlands of western Kenya was found appropriate and a better option as it requires less sophisticated infrastructure or highly trained personnel. The major requirement is the provision of affordable insecticide(s) and supervision of use of the same by public health/extension officers in rural areas. It is suggested that, targeted low coverage IRS be considered as a primary intervention strategy for malaria control in highland areas where diseases determinants are known and regularly assessed. Characteristics of malaria transmission in the study area that make it amenable to low coverage targeted IRS as a successful intervention strategy include seasonal and focal transmission and susceptibility of vector *A. gambiae s.s* to insecticide. Also, the local vector *A. gambiae s.s* had specific adaptations to feed on humans and showed a preference to breed in artificial/man-made habitats near human habitations resulting in ease of accessibility into houses and exposure to treated surface and/or make contact with man (Charlwood and Edoh, 1996; Minakawa et al., 1999). However, the same trait anthropophily makes *A. gambiae s.s* deadly as the vector of *P. falciparum* in many parts of Africa (Gillies and Warrel, 1993). The non-dispersed vector breeding sites and the associated aggregation of *A. gambiae s.s* in houses/shelters

near known breeding habitats (Lindblade et al., 2000) made the vector amenable to targeted IRS control. We concluded that, malaria control and prevention in the highlands of Kenya can benefit from an appropriate selection of control strategy based on the local circumstances and the capability of the intervention to reduce malaria risk in the wider community. In addition, it is important to continue to collect data on the effectiveness of these individual and/or combined interventions and its annual impact on endemic and epidemic malaria.

REFERENCES

American Red Cross (2002). Highland malaria sweeps Kenya mountain Towns. In the News, July 29, 2002.

Beier JC (1998). Malaria development in mosquitoes. In: Annual Rev. Entomol.. 43: 519-543.

Bermejo A Veeken H (1992). Insecticide-impregnated bed nets for malaria control: a review of field trials. Bulletin of the World Health Organization. 70: 293-296.

Bruce-Chwatt LJ (1985). *Essential Malariology*. London Heinmann. Second Edition. William Heinmann Medical Books pp 191-2.

Carter R, Mendis KN, Roberts D (2000). Spatial targeting of interventions against malaria. Bull. World Health Organ., 78(12): 1401-1411.

Charlwood JD, Edoh D (1996). Polymerase Chain Reaction used to describe larval habitat use by *Anopheles gambiae* complex (Diptera: Culicidae) in the environs of Ifakara, Tanzania. J. Med. Entomol., 33: 302-304.

Gillies MT (1954). The recognition of age-groups within populations of *Anopheles gambiae* by the pre-gravid and sporozoite rate. Ann. Trop. Med. Parasitol.. 48: 58-74.

Githeko AK, John MA, Peter KO, Francis KA, Bryson AN, John IG, Guiyun Y (2006). Topography and malaria transmission heterogeneity in western Kenya highlands: prospects for focal control. Malaria J., 5: 107.

Gilles HM, Warrell DA (1993). editors. In Bruce-Chwatt"s Essential Malariology. 3rd ed. London: Edward Arnold.

Guyatt, Helen L, Sarah KC, Timothy PR, Sam AO Robert WS (2002). Malaria prevention in highland Kenya: indoor residual house-spraying vs. insecticide-treated bed nets. Trop. Med. Int. Health, 7(4): 298-303.

Haddow AJ (1960). Studies on the biting habits and medical importance of East African mosquitoes in the genus *Aedes.* 1- Subgenera *Aedimorphus, Banksinella* and *Dunnius.* Bull. Entomol. Res., 51: 759-779

John CC, Brian D, Byrd, Francois XO (2004). Field assessments in western Kenya link malaria vectors to environmentally disturbed habitats during dry season. BMC Public Health, 4: 33.[http://creativecommons.org/licenses/by/2.0]

Kacey CE, Samson OA, Dickens OK, Mark LW, Chandy CJ (2006). Malaria hotspot areas in a highland Kenya site are consistent in epidemic and non- epidemic years and are associated with ecological factors. Malaria J., 5: 78-82.

Mulambalah CS (2009). Malaria vector studies with regard to the disease transmission and control in a highland area of Kenya. Ph.D Thesis 2009, Moi University, Kenya.

Killeen GF, McKenzie FE, Foy BD, Schieffelin C, Billingsley PF, Beier JC (2000). The potential impacts of integrated malaria transmission control on entomologic inoculation rate in highly endemic areas. Am. J. Trop. Med. Hyg., 62: 545-51.

Lindblade KA, Walker ED, Wilson ML (2000). Early warning of malariaepidemics in African highlands using *Anopheles* (Diptera: Culicidae) indoor resting density. J. Med. Entomol., 37: 664-674.

Lindsay SW, Martens WJM (1998). Malaria in the African highlands: past, present and future. Bull. World Health Organ., 76: 33-45.

MacDonald G (1957). Epidemics In: The epidemiology and control of malaria. London: London University Press.

Malakooti MA, Biomondo K, shanksGD (1998). Re-emergence of epidemic malaria in the highlands of western Kenya. Emerging Infectious Dis., 4: 671-676.

McMichael T, Githeko A (2001). Human Health. In Climate change 2001, Impacts, Adaptations and Vulnerability of Climate Change. Contribution of working Group 11 to the Third Assessment report of the Inter-governmental Panel on Climate Change. Scientific technical Analysis Edited by: McCarthy, J.J., Canzizni, O.F., Leary, N.A., Dokken, D.J., White, K.S. Cambridge university Press, Cambridge, United Kingdom; 2001: 451-485.

Minakawa N, Mutero CM, Githure JI, Beier JC, Yan G (1999). Spatialdistribution and habitat characterization of Anopheline mosquitoes in western Kenya. Am. J. Trop. Med. Hyg., 61: 1010-1016.

Minakawa N, Omukunda, Guofa Z, Githeko A, Guiyun Y (2006). Malaria vector productivity in relation to the highland environment in Kenya. Am. J. Trop. Med. Hyg,. 75(3): 448-453.

Molineaux L, Gramiccia G (1980). The Gaki Project. Geneva: WHO, 1980. Mulambalah C. S. (2009). Malaria vector studies with regard to the disease transmission and control in a highland area of Kenya. PhD Thesis, Moi University 2009, Kenya.

Najera JA, Zaim M (2001). Malaria vector control: insecticides for indoor residual spraying. WHO/WHOPES Document: WHO/CDS/WHOPES/2001.3.

Otsyula GM (2002). Population structure of *Anopheles arabiensis* breeding in transient and permanent inland habitats at two sites of western Kenya. M.Sc. Thesis (2002), Maseno University, Kenya.

Prybyski D, Khaliq A, Fox E, Sarwari A, Strickland G (1999). Parasite density andmalaria morbidity in the Pakistani Punjab. Am. J. Trop. Med. Hyg., 61: 791-801.

Romi R ,Razaiarimanga MC, Raharimanga R (2002). Impact of malaria control campaign (1993-1998) in the highlands of Madagascar: Parasitological and entomological data. Am. J. Trop. Med. Hyg., 66: 2-6.

Simon IH, Simba M, Busolo M, Abdisalan M, Noor HL Guyatt, SA, Ocholla, Rober WS (2002). Defining and detecting malaria epidemics in thehighlands of western Kenya. Emerging Infectious Diseases, 8(6): 1-14. [http://www.findarticles.com/p/articles/mi-moGVK/is-6-8/ai-87739659.]

Shanks GD, Biomondo K, Guyatt H, Snow RW (2005a). Travel and risk factor for uncomplicated *Plasmodium falciparum* malaria in the highlands of western Kenya. Transactions of the Royal Society of Trop. Med. Hyg., 99: 71-74.

Shanks DG, Simon IH, Judy AO, Robert WS (2005b). Malaria in Kenya's Western highlands. Emerging Infectious Dis., 11(9): 1425-1427.

Shililu L, Maier W, Seitz H, Orago A (1998). Seasonal density, sporozoite rates and entomological inoculation rates of *Anopheles gambiae* and *Anophelse funestus* in high altitude sugar growing zones in western Kenya. Trop. Med. Int. Health, 9: 706-710.

Snow RW, Gouws E, Omuombo J, Rapuoda B, Craig MA, Tanser FC, le Seur P, Ouma J (1998). Models to predict the intensity of *Plasmodium*transmission: application to the disease in Kenya. Transactions of the Royal Society of Trop. Med. Hyg,, 92: 601-606.

Some ES (1994). Effects and control of highland malaria epidemic in Uasin-Gisu District, Kenya. East Afr. Med. J., 71: 2-8.

Strangeways-Dixon D (1950). Paludrine (Proguanil) as a malarial prophylactic amongst African labour in Kenya. East Afr. Med. J., 27: 127-130.

Tropical Disease Research Progress Report 1997-98 Fourth Programme Report [TDR/PR14/99.1]

Thomson M (1996). Geographical perspectives on bet net use and malaria transmission in Gambia, West Africa. Social Sci. Med., 43: 101-

112.
Walker K (2002). A review of control methods for African malaria vectors Washington DC, US Agency for International Development, Activity Report 54.
World Health Organization (1963). Terminology of Malaria and of malaria eradication. Monograph Series No. 13. Geneva.
World Health Organization (1975). Manual on Practical Entomology in Malaria. Part II. Methods and Techniques. Volume 3. World Health Organization. Geneva, WHO (Offset publication No. 13.).

World Health Organization (1999). World Health Report: Rolling Back Malaria.

World Health Organization (2006). Global Malaria Program: use of indoor residual spraying for scaling up global malaria control and elimination. Document:WHO/HTM/MAL/2006.111