The Role of Aedes Mosquito in Yellow Fever Virus Transmission and its Control in Africas

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Research Article

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ABSTRACT

Throughout the world, many nuisance and potential transmitters of human and animal infections mosquitoes are distributing and occupying many biotopes. The female *Aedes* mosquitoes are commonly vectoring arboviruses by simply extracting blood from people, birds and other animals to obtain proteins needed to develop her eggs. Yellow fever virus, dengue virus, chikungunya virus, rift valley fever virus and zika virus are among the vector borne diseases. Understanding the competent vectors and the transmission cycle of yellow fever is the first step of collecting evidence since it provides suitable contribution for control strategies in different contexts.

The main objective of this paper was to review the ecological studies focused on yellow fever transmission by the major responsible vectors and what control methods are being performed in African regions. The differences in transmission of the virus with different mosquito species were reviewed from published documents. The circulation of yellow fever virus in the tropical regions of Africa relies on distinct hosts and vectors in sylvatic, rural or urban. The transmission of the virus among humans is associated with the presence of the vectors and unvaccinated population. The vectorial role can be influenced by the density, longevity and competence of the vector and associated environmental, behavioral, cellular and biochemical factors. *Aedes aegypti, Aedes africanus, Aedes luteocephalus, Aedes bromeliae, Aedes furcife* and *Aedes taylori* have been shown to be the main vectors of yellow fever. The two core control strategies of yellow fever are vector control that requires a constant effort wherever the risk of vector development is high and immunization/vaccination of populations at risk. Chemical, biological and environmental sanitation are the best and frequented control methods in Africa. Integrated control taking into account sanitation and mutualized with other vector borne diseases, is cost effective and should be favored.

Keywords: *Aedes* mosquito ; Yellow fever ; Transmission; Control; Africa

INTRODUCTION

Throughout the world, many nuisance and potential disease transmitters of human and animal infections mosquitoes are distributing and occupying many biotopes. Many viruses transmitted by these mosquitoes are affecting humans and animals. From all mosquitoes, *Aedes* is considered as one of the most relevant groups of mosquito in public health and got interest because of their role in the transmission of many arboviral diseases, causing large-scale outbreaks throughout the world. Yellow Fever Virus (YFV), Dengue Virus (DENV), Chikungunya Virus (CHIKV), Rift Valley Fever Virus (RVFV) and Zika Virus (ZKV) are among the vector borne diseases. The viruses can be transmitted through the bite of infected mosquito vectors during blood meal on human and handling tissues and body fluids of infected patients. Members of the *Aedes* genus are known vectors for numerous viral infections. Stegomyia is the most important subgenus of *Aedes* under subgenera of mosquito from stand point of the transmission of pathogens. *Aedes* mosquitoes are commonly vectoring arbo-viruses. The female *Aedes* acquires and transmits the virus by simply extracting blood from people, birds and other animals to obtain proteins needed to develop her eggs. This indicated that the viruses have zoonotic importance, having major consequences for public health and economic productivity. Many of them cause severe and potentially fatal illness in humans. The outbreaks of arbo-viral diseases, the rapid spread and increasing challenge in Africa is posed by mosquito-borne viruses. This constitutes serious health, economic and social problems [1].

The circulation of YFV currently in the tropical regions of Africa, primarily maintained through a sylvatic cycle between non-human primate hosts and sylvatic mosquito vectors. In Africa, the frequency of epidemics and the adaptation of the YFV to its hosts and vectors argue for an older presence. Based on resemblance for their respective vector, there are five genotype of YFV in Africa. Two strains, east African which diverged from an ancestral Flavivirus and west African separated from east African ones about three centuries. YFV transmission relies on distinct hosts and vectors in the old world (Africa) which can be in sylvatic, rural or urban, with occasional large outbreaks in urbanized regions. The sylvatic vectors of *Aedes africanus* group and other *Aedes* species belonging to several subgenera and non-human primates are responsible for the transmission of YF [2].

High transmission of YF virus among humans is associated with the presence of the vectors and unvaccinated populations. Sporadic YF infection occurs almost exclusively in forestry and agricultural workers because of occupational exposure. High densities of mosquito vectors (*Aedes* and *Haemagogus*) closer to human dwellings and reservoir hosts within unvaccinated and highly populated areas are also other factors expanding the geographical spread of this virus. *Aedes* mosquito, the vector of YFV are originated in Africa where numbers of primate species are infected. The capacity of disease transmission can be determined by the degree of anthropophily. Vectorial capacity of the *Aedes* mosquito species is used to determine the ability mosquito to serve as a disease vector. The vectorial role can be influenced by the density, longevity and competence of the vector. In addition, associated environmental, behavioral, cellular and biochemical factors influence its association between the virus and host. Competent *Aedes* mosquitoes determine the establishment of a local YF transmission cycles outside endemic areas. This is due to active *Aedes* mosquitoes all year long in tropical regions and during the warm period in temperate areas. In genus *Aedes*, for example: In terms of transmission potential, sylvatic-cycle vectors are more efficient than those of the urban cycle. Some species, for example, *Ae. albopictus* are anthropophilic in nature and they are densely populated in urban areas which allow them to be a vector of YFV. During YF outbreaks, *Ae. aegypti*, *Ae. africanus*, *Ae. luteocephalus*, *Ae. bromeliae*, *Ae. furcifer* and *Ae. Taylori* have been shown to be the main vectors. Some other species play a secondary role, while the other species play subsidiary roles. Understanding the competent vectors and the transmission cycle of YF in occurrence of outbreaks is the first step of collecting evidence since it provides suitable contribution for control strategies in different contexts. The two core control strategies of YF are vector control that requires a constant effort wherever the risk of vector development is high and immunization/vaccination of populations at risk based on selective strategy. Integrated control taking into account sanitation and mutualized with other vector borne diseases, is cost effective and should be favored [3].

The main objective of this paper was to review the ecological studies focused on YFV transmission by the major responsible vectors and what control methods are being performed in African regions. The differences in transmission of the virus with different mosquito species has well reviewed from published documents [4].

LITERATURE REVIEW

PubMed and all published documents on known journal were searched using the terms "*Aedes* mosquito". Articles found were searched for the descriptions of the original research articles about *Aedes* mosquito's roles in YF virus transmission. All World Health Organization reports, guidelines and archives were searched online through Google based on the subject matters. This search has supplemented by identification of reports that formed part of post-graduate thesis and more traditional bibliographic searches of peer-reviewed literature and fact sheets [5].

Yellow Fever (YF) burden in Africa

Yellow fever (YF), a deadly viral disease caused by *Flaviviridae*. The disease became a major problem in the colonial settlements of the Americas and west Africa in the 1700s and was repeatedly introduced into sea ports of the United States and Europe during this time. The virus symptoms includes jaundice, enlargement of the liver and in several cases hemorrhage. According to viral genome sequence analysis, YFV originated in Africa about 3000 years ago. In 1648, the earliest record of an epidemic was in the Yucatan in Mexico spread to other countries through the slave trade and is maintained in enzootic cycles involving monkeys and mosquitoes in 34 countries of Africa [6].

YF is known to be endemic in tropical and sub-tropical areas of South America and Africa. As of annual WHO estimate, 90% of the infection occurring in African from over all 200,000 cases of YF and 30,000 deaths. The number of YF cases has been increasing since 1980s, which can be attributed to improved surveillance systems and better access to laboratory services. For example, between 1984 and 1990 about 22,647 cases were reported from Africa, of which 21,299 were from Nigeria. In the year 2013, the estimated number of YF burden in Africa was 130,000 cases and 78,000 deaths. In the same year, 230 cases of YF (including 85 deaths) were reported to WHO from four African countries: Ethiopia, Sudan, Democratic Republic of Congo (DRC) and Cameroon. Of this report, 206 cases and 69 deaths were mainly from Ethiopia and Sudan, but also from the Democratic Republic of Congo and Cameroon. In 2014, seven cases and two outbreaks were reported from DRC. Ongoing yellow fever epidemic has reported in Angola since December 2015 and an outbreak was officially declared in January 2016 by WHO. In 2016, 884 cases and 373 deaths were reported. The disease was spread to Kenya and the DRC. In DRC 76 cases and 16 deaths were recorded in the year 2016. Seven confirmed cases from Uganda, four cases from Republic of Congo, two cases from Sao Tome and Principe, one case from Ethiopia, four sylvatic considered cases from Ghana and 39 confirmed case from Guinea were reported within the same year [7].

Role of *Aedes* mosquito in YF transmission in Africa

Across regions of Africa, the vectors and associated ecological patterns of YFV transmission is different. Historically dynamics interest in the mosquitoes of Africa has been derived from their ability to thrive mostly in the tropics and act as the vectors of the most debilitating human diseases caused by bio-agents. The two most prominent vectors of YFV are *Ae. aegypti* and *Ae. albopictus* which also transmit zika, dengue fever, west nile fever, chikungunya and eastern equine encephalitis. During the 16th century, the YFV and its mosquito vector transported on ships sailing from West Africa to the West Indies. Generally, humans may become infected by exposure to vectors that have acquired infection from monkeys. YFV carried to and ravaged much of the eastern regions of the Americas later by coastal shipping of both the vector and infected humans [8].

In Africa, nearly all mosquito species implicated in YFV transmission belong to the genus *Aedes* (sub genera *Stegomyia* and *Diceromyia*). The major *Aedes* mosquito species transmitting YF include *Ae. aegypti*, *Ae. africanus*, *Ae. luteocephalus*, *Ae. simpsoni* complex, Ae. furcifer, *Ae. taylori* and *Ae. vittatus* (belong to subgenus *Aedimorphus*). In parts of Africa (East Africa), during YF epidemic, the current most important vector is *Ae. simpsoni sensulatu* (s.l.) likely *Ae. bromeliae*, which was the principal vector during the largest recorded epidemic of yellow fever in Ethiopia in between 1960 and 1962. YFV is maintained in three transmission cycles. In the urban cycle, YFV is featured between humans by domesticated *Ae. aegypti*. In the sylvatic cycle, the virus is maintained by tree hole-breeding *Ae. africanus* mosquitoes feeding on monkeys [9].

Urban transmission of YF

Aedes aegypti mosquito is a tropical primary vector of urban YFV that has recently established at many geographic locations due to globalization and a warming climate. In the tropics of Africa and America, *Ae. aegypti* largely feeds blood on human and is a classical vector of urban YF. *Ae. aegypti* is a domestic and genetically distinct with discrete geographic niches originated in Africa from its ancestral form *Ae. aegypti* formosus, a zoophilic tree hole mosquito. Due to anthropophilic, endophagic and endophillic behavior, *Ae. aegypti* is domestic mosquito. The vectorial capacity of *Ae. aegypti* is influenced by the density, longevity and competence of the vectors. Moreover, the association between the virus type and host is influenced by environmental, behavioral, cellular and biochemical factors. Though the population of *Ae. aegypti* occurs throughout the tropics and subtropics, the ability to transmit disease varied place to place. For instance, across sub-Saharan Africa, some populations are less strongly human associated, being found in forests, ovipositing in tree holes and feeding on other mammals; whereas other populations are domestic, breeding in water in and around homes and feeding on humans. Outside Africa, *Ae. aegypti* has a strong genetic preference to feed blood on humans in the houses. They also have an ability to survive and oviposit in relatively clean water in manmade containers in the human environment. After YFV is introduced to humans, inter-human transmission can be sustained, amplified and transmitted in dry habitats and urban areas where water is stored in containers by the domestic *Ae. aegypti*. The genetic factors and inherent tolerance of the vector ensuring viral transmission, infection and replication [10].

In the urban cycle, the most deadly form of disease spread, potentially linking thousands of human cases is transmitted from human to human as a result of *Ae. aegypti*. The *Ae. aegypti* is highly domesticated and often found in close humans dwellings especially in urban settings, as opposed to the more zoophilic genetic form *Ae. aegypti* formosus. In West Africa, the domestic mosquito, *Ae. Aegypti*, found experimentally to be a relatively in efficient vector of the virus for epidemic spread of YFV. The anthropophilic nature of this species combined with its high densities in urban areas to overcome its low vectorial capacity. Within the sylvatic cycle, *Ae. aegypti* formosus is involved in the transmission of YF in non-human primates. In urban cycles, in larger outbreaks of YFV and further spread of YFV to dry in more populated areas by highly anthropophilic, *Ae. aegypti* and its trans-ovarial transmission. The virus received from sylvatic cycle featured by wild mosquito. Sylvatic YFV has emerged from the sylvatic cycle into urban transmission cycles among humans [11].

Sylvatic transmission of YF

Ae. africanus is the dominant species that found in forest areas and in forest galleries of savannah regions of east and central Africa. Its distribution is more localized in West Africa. *Ae. africanus* is primatophilic, very aggressive to humans and bites preferentially in the forest canopy and ground level. In the great rainforests of central Africa and extending outward along riverine forests, the main role of *Ae. africanus* mosquitoes are serving as a the primary vector of sylvatic YFV transmission. *Aedes africanus* is associated with sylvan habitat throughout Africa that breeds in water filled tree holes, stump holes and cut bamboo in the forest and in artificial containers. In some locations of Africa, for example, Nigeria, *Ae. africanus* commonly found in villages in addition to forest habitat. This raises the possibility that some populations of *Ae. africanus* are better adapted to domestic environments. Including *Ae. africanus*, there are other species involved YF transmission are *Ae. opok*, *Ae. metallicus*, *Ae. bromeliae*, *Ae. vittatus*, *Ae. luteocephalus*, *Ae. taylori*, *Ae. furcifer* and *Ae. simpsoni* complex. The natural breeding sites of these all species are the same rain waters with common primatophilic feeding habits and host seeking behavior in the forest canopy. In west and central Africa, under laboratory condition, *Ae. africanus* is an efficient YF vector and the virus has also been isolated from natural populations. *Ae. africanus* will readily bite man within the forest at ground and canopy level and near human settlements. *Ae. africanus* found to bite humans in and outside of houses and are described as anthropophilic in Africa. *Ae. africanus* is known to feed on monkeys and crepuscular in its biting activity through moving from ground level to the canopy [12].

In central Africa, *Ae. opock* could be considered as a major YF vector because of its high densities, which sometime exceed that of *Ae. africanus*. *Ae. pseudoafricanus* and *Ae. neoafricanus*. These species involved in the wild cycle of transmission but tend to play a minor role because of their rarity. *Ae. opock* is found in the forested regions of central Africa participated in the local spread of the virus, displaying similar transmission dynamics with limited sporadic human cases with *Ae. africanus*. As in central and east Africa, both species remains the main sylvatic vector for YFV in West Africa [13].

Savannah transmission of YF

The intermediate or savannah cycle involves such tree hole breeding mosquito species such as *Ae. luteocephalus, Ae. furcifer*, *Ae. metallicus*, *Ae. opock*, *Ae. taylori*, *Ae. vittatus* and members of the *Ae. simpsoni* complex spread to humans living or working in jungle border areas in Africa. *Ae. luteocephalus* is another species of the subgenus *Stegomyia*, which is morphologically similar to *Ae. africanus*. It is simio-anthropophilic, has a crepuscular behavior and takes blood meals at the canopy, but occasionally bites on the ground. This species is abundant in forest habitats and may be present in very rare situations in the villages surrounding the forest. It is one of the major vectors of YF in West Africa and has been confirmed in various outbreaks [14].

Aedes vittatus plays an important role in the maintenance and transmission of YF as an important vector in Africa. Because of abundance, anthropophilic behavior and high susceptibility and competence to transmit YFV, *Ae. vittatus* pose a major threat to public health in Africa. Throughout tropical regions of Africa, Asia and the mediterranean region of Europe, *Ae. vittatus* mosquito is a hungry biter of humans and predominantly a rock-hole breeder as well in diverse macro and micro-habitats. *Ae. vittatus* has the potential to expand its distribution and abundance due to its ability to adapt to human dwellings using available breeding habitats, such as domestic containers, in absence of its preferred breeding sites. In Africa, *Ae. vittatus* is predominantly found in canopy (sylvatic), forest ground or peridomestic in rural. Experimentally, it has been implicated as an important and potential vector of YFV in several African countries. In most African regions, several isolations of the virus from *Ae. vittatus* mosquitoes have been made and the highly susceptibility of this mosquito to yellow fever is confirmed. The infected mosquito has been successfully capable of demonstrating the transmission of yellow fever to monkeys [15].

Ae. simpsoni consists of a complex of mosquito species responsible for YFV transmission. According to studies, there are three sibling species of the *Ae. simpsoni* group: *Ae. simpsoni sensustricto*, *Ae. bromeliae* and *Ae. lilii*. The role of these sibling species in YF virus transmission have also been clarified. *Ae. lilli* does not play a role in YF virus transmission to humans because of its zoophilic tendency and distributed from Southeast Sudan to western Ethiopia crossing to south to northern Uganda. This species is relatively uncommon compared to *Ae. bromeliae* and have only been reported from leaf axils of *Sanseuieria spp*. in Uganda.

*Aedes simpsoni*s.l. breeds in plant leaves and tree holes which are abundant in forests and in transition areas of forest and savannah with heavy rain falls. *Ae. simpsoni* that restricted to Southern Africa is known to bite man. According to precipitin analysis, all blood meal samples from *Ae. simpsoni*s.l. were mammalian origin. In 1941 in Uganda, *Ae. simpsoni* was incriminated in the transmission of yellow fever virus during outbreak of YFV. The virus has also been isolated from wild caught mosquitoes in this country. Among the three species of *Ae. simpsoni*, *Ae. bromeliae* is an important vector of Yellow Fever Virus (YFV) and potentially other arboviruses in East Africa. In Central Africa, *Ae. bromeliae* is a suspected vector of YF virus because of its close interaction with humans. This mosquito is highly aggressive during the afternoon and sometimes bites at dusk and early in the morning. In West Africa, *Ae. bromeliae* is prevalently distributed with zoophilic behavior; it does not seem to play a role in YF transmission to humans. The natural breeding sites of *Ae. bromeliae* are plant leaves, tree holes, fruit husks and containers in the domestic and peri-domestic environment. *Aedes bromeliae* preferably feed on human hosts for their blood meal, maintaining the virus in the rural cycle in East Africa.

DISCUSSION

Control strategies

Strategies for prevention of YF infections depend on either control of vectors or active immunization of population with vaccine. Both vector surveillance and control are components of the prevention and control of vector borne diseases transmission. This is an important step in *Aedes mosquito* control operations through identifying the types and abundance of containers producing mosquitoes. Using pesticides is an integral part and the most immediate method of controlling mosquitoes. The best long term controls of *Aedes* mosquito can be changed from chemical based control to non-chemical approaches because of lack environmental safety and resistances. Pesticides should serve as a supplement to these control methodologies since it is the only practical technique to manage massive mosquito outbreaks or to reduce the threat of disease. Traditionally, mosquito killing using a lot of chemicals or insecticides is a major vector control. Space spraying, residual spraying, barrier spraying and using attractive toxic baits are chemical control methods used for adult mosquitoes. Placing chemicals or other control agents in mosquito breeding habitats for killing of immature (larvae) *i.e.* larviciding is effective and environmentally safe. Many of these products use either bacterial toxins or insect growth hormones to kill the larvae or block their development. Environmental management as reduction or removal of mosquito breeding sites has often been used together with chemical or microbiological control strategies in areas where endemic mosquito-borne diseases occur. Because of development of insecticide resistance, the damage to the environment and effects on non-target organisms are becoming a concern that limit the use of synthetic insecticides. It is therefore not surprising that interests in alternative non chemical strategies has increased over the last decades. Environmental sanitation involves elimination of containers producing *Aedes* by various means. Within adult population, suppression of vector population is the best method that aimed to reduce the number of disease-transmitting mosquitoes through substituting wild type mosquitoes with ones that have impaired vector competence in order to block pathogen transmission. For instance, *Wolbachia* (safe for human and environment) is extremely common bacteria that occur naturally in insect and best to suppress mosquitoes. Entomopathogenic fungi which are naturally occurring organisms that are pathogenic to mosquitoes can also be considered for biological control strategies. *Bacillus thuringiensis var. israelensis* is currently the most common mosquito larvicide employed in European countries now coming to Africa. Entomopathogenic fungi produce infective spores (conidia) that attach to and penetrate the cuticle of mosquitoes, releasing toxins that result in mosquito death. *Lagenidium, Coelomomyces* and *Culicinomyces* are among important genera of mosquito pathogenic fungi to kill both larvae and adult stage. Therefore, the evolution of fungus resistance is predicted to be much slower than the evolution of insecticide resistance. Fish species are also found effective in controlling *Ae. aegypti* larvae in a variety of containers around homes. Fish species known to larvivorous and herbivorous potentials in different regions of the world. The promising larvivorous fish belong to the families *Poecilidae, Cyprinidae* and *Chichlidae*. Integrated control taking into account sanitation and mutualized with other vector borne diseases, is cost effective and should be favored. Integrated Vector Management (IVM) is a new and better approach to vector control. IVM is important in decision-making process for optimizing resources through a careful analysis of the local ecology of the vector-borne diseases.

CONCLUSION

The circulation of YFV currently in the tropical regions of Africa is primarily maintained through a sylvatic cycle between its non-human primate hosts and sylvatic mosquito vectors. Yellow fever is known to be endemic in tropical and sub-tropical areas of Africa with 90% of the infection. In Africa, the major *Aedes* mosquito species transmitting YF include *Ae. aegypti*, *Ae. africanus*, *Ae. luteocephalus*, *Ae. simpsoni* complex, *Ae. furcifer*, *Ae. taylori* and *Ae. vittatus*. In parts of Africa (East Africa), during epidemic YF, the current most important vector is *Aedes simpsoni sensulatu* (s.l.) likely *Ae. bromeliae*, which was the principal vector during the largest recorded epidemic of yellow fever in Ethiopia in between 1960 and 1962. YFV is maintained in three transmission cycles. Urban cycle, in which YFV is featured between humans by domesticated *Aedes aegypti*. Sylvatic cycle in which the virus is maintained by tree hole-breeding *Ae. africanus* mosquitoes feeding on monkeys and savannah cycle, in which the virue is maintained by tree hole breeding mosquito species, *Ae. luteocephalus*, *Ae. furcifer*, *Ae. metallicus*, *Ae. opock*, *Ae. taylori*, *Ae. vittatus* and members of the simpsoni complex spread to humans living or working in jungle border areas in Africa. The control methods of *Aedes* mosquitoes include chemical, biological and environmental sanitation. In Africa, the best and frequented control methods are chemical and environmental sanitation. Integrated Vector Management (IVM) is a new and better approach to vector control.

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