Chapter 3

Ecology of *Aedes* Mosquitoes, the Major Vectors of Arboviruses in Human Population

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Additional information is available at the end of the chapter

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Abstract

Aedes aegypti (Stegomyia) has been human vectors for many human diseases globally. In recent years, dengue virus has been diagnosed in different regions such as Asia and Latin America vectored by *Aedes* spp. mosquitoes. Dengue cases have been reported again in the several parts of African and other continental hospital. The different types of breeding sites have been found to be abundant in both urban and rural areas. The abundance of adult *Ae. aegypti* and habitat productivity in different settings escalates the risk of dengue transmission if viruses are found in asymptomatic population. The insecticide resistance has been found to occur in the wild population of *Aedes aegypti* to insecticides commonly used for indoor residual spray and long-lasting insecticidal net treatments. The control of human vector population is still a challenge as the vector has a diurnal feeding and outdoor resting behavior. Environmental management is still the best practice to be adopted in many countries for *Aedes aegypti* control. The currently discovered dengue vaccine might be an immediate arsenal for the community immunization.

Keywords: *Aedes aegypti*, ecology, insecticide resistance, control, arboviruses

1. Introduction

Mosquitoes are small, midge-like flies that constitute the family Culicidae. Females of most species are ectoparasites feeding on vertebrates' blood through piercing the hosts' skin to suck the blood. To-date, approximately 3500 species of the Culicidae have been described. The family Culicidae is a large and abundant group which occurs throughout temperate and tropical regions of the world and well beyond the Arctic Circle [1]. There are two subfamilies of Culicidae, that is, the Anophelinae (3 genera) and the Culicinae (110 genera). The subfamily Culicidae, *Aedes* is the largest tribe of mosquitoes with 1256 species classified into 10 genera: Aedes sensu (931), Armigeres (58), Eretmapodites (48), Haemagogus (28), Heizmannia (38), Opifex (2), Psorophora (49), Udaya (3), Verrallina (95), and Zeugnomyia (4) [2].

The public health concern of *Aedes* mosquitoes particularly *Ae. aegypti* and *Ae. albopictus* in the transmission of arboviruses such as dengue virus, chikungunya virus, ZIKV virus, and yellow fever virus is kept on increasing globally. Over half of the world's population is at risk of dengue and chikungunya infections [3]. The Caribbean, South America, and Europe are no longer spared from chikungunya infection, a disease which was previously limited to Africa and Asia [3]. According to the World Health Organization, about 2.5 billion people globally live in dengue endemic regions [4]. Dengue is the most worldwide important mosquito-transmitted viral infection [4]. Over 100 countries in Africa, North and South America, Southeast Asia, Europe, and the Pacific are reported to have had severe dengue outbreaks [5]. The annual occurrence of dengue fever infections ranges from 50 to 100 million with which around 500,000 facing severe morbidity causing to over 20,000 mortalities, pediatrics beings the most cases [5]. The chikungunya virus infections (CHIKV) have been documented in over 60 countries in Asia, Africa, Europe, and the Americas [6]. The estimated number of chikungunya cases in Americas in 2016 was 693,000, and Zika virus (ZIKV) disease was 500,000 [6, 7]. Yellow fever cases in Africa were 130,000 with an estimated 31,000 annual disability adjusted life years and 500 deaths [8, 9].

About 80% of the world's population is at risk for at least of exposure to one vector-borne disease; these diseases account for about 17% of the estimated global burden of communicable diseases and cause over 700,000 deaths annually, affecting disproportionately poorer populations [6, 9]. They hamper economic development through direct medical costs and indirect costs such as the loss of productivity and tourism. The social, demographic, and environmental factors strongly influence transmission patterns of vector-borne pathogens. Vector control is an important component for decision science in the prevention and control of vector-borne disease approaches. Consequently, the global distribution and ecology of these vectors and the geographical determinants of their ranges are essential in order to be effective. Therefore, it is important to work out where these mosquito species are found around the globe to identify the areas at risk. It is also important to predict where these species could become established if they were introduced, in order to identify areas that could become at risk in the future.

1.1. *Aedes* distribution

Ae. aegypti and *Ae. albopictus* are worldwide distributed between 35° N and 35° S, latitudes that roughly correspond to a 10°C winter isotherm which appears to be the limiting temperatures that the species can tolerate while overwintering [5]. The species are highly adapted to urban environments, breeding in stagnant water found in manufactured containers, garbage heaps, and tyres. However, the distribution of *Ae. albopictus* has been highly biased to temperate climates [10] though the vector is now widely distributed throughout the Americas (excluding Canada), Europe, Asia, Africa, Australia, and the Pacific [11].

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The geographic distribution of *Ae. aegypti* based on the order of higher levels of occurrence for each continent reveals that in the Americas, the Brazil ranks the highest (**Table 1**). In Africa, occurrence of the vectors have been recorded in Senegal, Cameroon, Kenya, Tanzania, Ivory Coast, Nigeria, Madagascar, Gabon, and Sierra Leone (**Table 1**). In Asia/Oceania, occurrence of *Ae. aegypti* has been reported and documented (**Table 1**) [3, 12].

1.2. Ecology of *Aedes* mosquitoes

1.2.1. Aedes aegypti

Ae. aegypti is an arthropod closely associated with humans and their habitats. They are mostly anthropophilic [13] with high preference to the urban environment [14]. They get blood meals from human, and human creates conducive environment for their population growth through up haphazardly disposal of water-holding containers/obsoletes around our homes. The mosquito lays her eggs on the sides of containers with water, and eggs hatch into larvae after a rain or flooding. A larva changes into a pupa in about a week and into a mosquito in 2 days. The *Aedes* main habitat is aquatic, and they can thrive better from tree cavities to toilets. People also furnish shelter as *Ae. aegypti* preferentially rests in darker cool areas, such as closets leading to their ability to bite indoors.

Ae. aegypti has adaptations to the environment that makes them highly resilient, or with the ability to rapidly bounce back to initial numbers after disturbances resulting from natural phenomena (e.g., droughts) or human interventions (e.g., control measures). One such adaptation is the ability of the eggs to withstand desiccation (drying) and to survive without water for several months on the inner walls of containers. For example, if we were to eliminate all larvae, pupae, and adult *Ae. aegypti* at once from a site, its population could recover 2 weeks later as a result of egg hatching following rainfall or the addition of water to containers harboring eggs.

It is likely that *Ae. aegypti* is continually responding or adapting to environmental change. For example, it was recently found that *Ae. aegypti* is able to undergo immature development in broken or open septic tanks resulting in the production of hundreds or thousands of *Ae. aegypti* adults per day. In general, it is expected that control interventions will change the spatial and temporal dispersal of *Ae. aegypti* and perhaps the pattern of habitat utilization.

1.2.2. Aedes albopictus

Aedes albopictus (*Stegomyia albopicta*), from the mosquito (Culicidae) family, also known as (Asian) tiger mosquito or forest mosquito, is a mosquito native to the tropical and subtropical areas of Southeast Asia; however, in the past few decades, this species has spread to many countries through the transport of goods and international travel [15]. The eggs of *Ae. albopictus* are desiccation resistant, which enhance survival in inhospitable environments [16]. *Ae. albopictus* is among the aggressive outdoor species of mosquito, and they are day biter that has a very broad host range and attacks humans, livestock, amphibians, reptiles, and birds [17]. Their biting rate level can be as high as 30 to 48 bites per hour [18]. *Ae. albopictus* survives at a large range of temperatures [19].

	Country	Occurrences		Country	Occurrences		Country	Occurrences
Ae. aegypti								
Americas	Brazil	5044	Europe/ Africa	Senegal	112	Asia/ Oceania	Taiwan	9490
	USA	436		Cameroon	55		Indonesia	603
	Mexico	411		Kenya	52		Thailand	495
	Cuba	177		United Republic of Tanzania	44		India	423
	Argentina	170		Côte d'Ivoire	40		Australia	282
	Trinidad and Tobago	152		Nigeria	35		Viet Nam	223
	Venezuela	130		Madagascar	28		Malaysia	112
	Colombia	128		Gabon	27		Singapore	44
	Puerto Rico	120		Mayotte	20		Philippines	36
	Peru	89		Sierra Leone	20		Cambodia	29
Ae. albopictus								
Americas	Brazil	3441	Europe/ Africa	Italy	203	Asia/ Oceania	Taiwan	15,339
	USA	1594		Madagascar	58		Malaysia	186
	Mexico	50		Cameroon	42		Indonesia	161
	Cayman Islands	15		France	37		India	150
	Haiti	13		Gabon	27		Japan	97
	Guatemala	12		Albania	22		Thailand	82
	Venezuela	7		Mayotte	21		Singapore	44
	Colombia	3		Greece	18		Lao People's Democratic Republic	26
	Cuba	3		Israel	17		Philippines	22
	Puerto Rico	3		Lebanon	15		Viet Nam	18

Note: This table was contributed by Kramer a leading author of the paper published in E-life journal (https://doi.org/10.7554/eLife.08347.003).

Table 1. The ***Aedes aegypti*** and ***Ae. albopictus*** distribution globally.

Ae. albopictus is a treehole mosquito, and so its breeding places in nature are small, restricted, shaded bodies of water surrounded by vegetation. It inhabits densely vegetated rural areas. However, its ecological flexibility allows it to colonize many types of man-made sites and urban regions. It may reproduce in cemetery flowerpots, birdbaths, soda cans and abandoned containers, and water recipients. Tyres are particularly useful for mosquito reproduction as they are often stored outdoors and effectively collect and retain rainwater for a long time. The addition of decaying leaves from the neighboring trees produces chemical conditions similar to tree holes, which provides an excellent substrate for breeding. *Ae. albopictus* can also establish and survive throughout nonurbanized areas lacking any artificial containers, raising additional public health concerns for rural areas [17].

1.2.3. Aedes mosquitoes life cycle

Aedes mosquito species, *Ae. aegypti*, and *Ae. albopictus* are major public health concern due to their role in transmission of diseases [3]. *Ae. aegypti* mosquito is widespread in (sub-)tropical regions and is largely responsible for vector-borne arboviral infections, yellow fever virus (YFV), ZIKV, dengue virus (DENV), West Nile virus (WNV), CHIKV and transmission, and outbreaks in various regions [3, 7]. The *Ae. aegypti* is known to have high vectorial capacity due to its anthropophilic behavior, well domesticated, and adapted to survive in different geographical regions including Africa, Americas, Asia, and Europe [1, 3].

The *Aedes* spp. mosquitoes are known to have a complex life cycle involving aquatic and terrestrial life [2]. Mosquitoes acquire the infection after a blood-meal form the host in order for the eggs to develop. The vector needs water to lay their eggs in the preferred breeding container, including tyres, water storage containers, disposed tyres, coconut shells, and flowerpots [20]. *Aedes* spp. prefers to lay their eggs on the inner wet walls of containers with water, hence the name “container breeder”. The development of the eggs occurs between 2 and 7 days in the aquatic phase (**Figure 1**) where the larvae hatch from the eggs. The larva survival depends on the microorganisms found in the aquatic environment. Larvae go through developmental stages (stage 1–4) in which they molt or shed their skin; these larval stages are called the first to fourth instars [20]. When a larva is a fully grown fourth instar, it undergoes metamorphosis into a new form called a pupa in approximately 4 days, the “cocoon” stage for the mosquito. This developmental stage of the mosquitoes also occurs in the aquatic environment. After 1–2 days, the fully developed adult mosquito forms and breaks through the skin of the pupa and a fully grown adult emerges. The adult mosquito is able to fly and has a terrestrial habitat inhabiting inside and outside households [20].

Interestingly, *Aedes* has developed a survival mechanism during the dry seasons; the eggs can enter a dormancy (quiescence) for up to 8 months at the end of embryogenesis [21]. If the habitat is dry, the eggs remain dormant but after rainfall, the eggs hatch and development continues [20]. In addition to being desiccation resistant, *Aedes* spp. is well adapted to produce, eggs can withstand months of dormancy, so-called “extended quiescence” in the unfavorable abiotic environment [21]. The male *Aedes* spp. mosquitoes feed on flowers’ nectar or plant juices, unlike the female that needs a blood meal [22]. The vector becomes infected

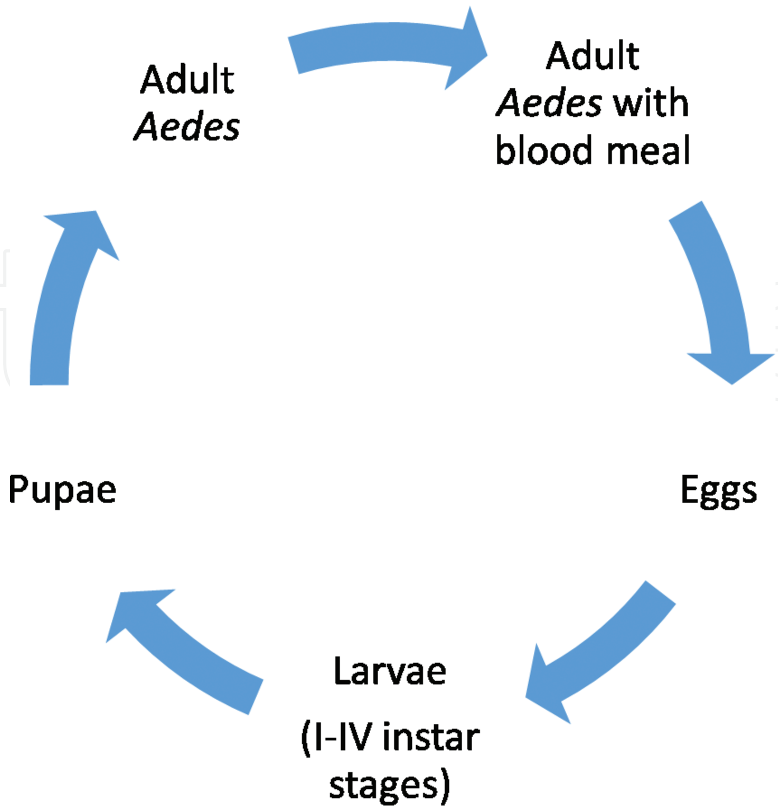

Figure 1. *Aedes* mosquito life cycle in aquatic and terrestrial phases.

when they feed on infected humans, and transmission may occur when the vector bites the host, which is believed to be promoted by mosquito salivary protein.

Historically, *Ae. aegypti* is believed to have originated from zoophilic subspecies *Ae. Aegypti formosus* inhabiting forests in sub-Saharan Africa [12]. This subspecies is found in the forests, breed in the tree holes and feeding on other mammals. The evolution of the ancestral *Ae. aegypti* resulted in the domesticated *Ae. aegypti* subspecies with a strong preference for biting humans and breed in man-made containers [20]. This evolved as the dominant vector of several diseases including yellow fever and DENV, ZIKV infections worldwide. The domestication of the vector was associated with the human migrations, trade, transportation, and urbanization [20, 23]. The domestic *Ae. aegypti* thrive in (sub-)tropical and temperate regions and can inhabit either terrestrial or aquatic depending on the stages of the growth. *Ae. aegypti* is primarily a container breeding vector and is known to predominate in urban areas where there is the vast composition of favorable man-made breeding container environment [20]. The breeding sites range from natural to artificial including vegetation, discarded tyres, discarded containers, bottle tops, water storage containers (especially in places with erratic tap water supply), flowerpots and vases, metal drums, and coconut shells [9, 24]. Other breeding sites include the open or unsealed septic tanks, water wells, and water meters. The ecological factors determine the crucial characteristics of different stages of the life and eventually its success. The *Ae. aegypti* larvae feed on nutritious materials available in the aqueous phase in the breeding containers including the plant particles, animal debris, and phytoplankton such as microalgae found in the water-filled containers [25]. The ecological characteristics are important in the life cycle of the adult vector including the longevity, fecundity body mass, and vectorial competence [26]. For instance, some algae species, *Cladophora sp*., *Chlorella ellipsoidea*, and *Rhizoclonium hieroglyphicum*, were shown to exhibit larvicidal properties that affect the development of the immature stages [25]. Evidence suggests that the developmental stage from first instar larval stage to adult mosquito is faster when the organic matters are abundant in the breeding container, in addition, the survival rate of the immature stage is enhanced [27]. In contrast, low concentration or exhaustion of the nutrients is required to trigger pupation presumably in response to the increasing level of ecdysteroid hormone [3, 28, 29]. Temperature is important for the survival larva density and competence of the *Ae. aegypti*. In areas where the temperature is warmer, the development of the aquatic stage temperature was associated with shorter development time from hatch to the emergence of the adult mosquito [4]. Similarly, longer light exposure was also shown to shorten the development time [30]. The evidence explains the widespread distribution and pattern of *Ae. aegypti* in (sub-)tropical regions. Furthermore, evidence suggests increasing *Ae. aegypti* abundance in urban areas leading to outbreaks [31]. It is evident that developing countries are becoming more urbanized; however, poor city planning and sanitation have increased mosquito breeding sites [7]. The "ecological plasticity" exhibited by the vector is arguably among the reasons for reason that explain it its worldwide widespread and success as a human vector.

1.3. Insecticide resistance in *Aedes* spp.

The emergence of insecticide resistance to multiple classes of insecticides has been widely reported in *Ae. aegypti* in different regions [24, 32–34]. WHO defines resistance as the ability of mosquitoes to survive exposure to a standard dose of insecticide; this ability may be the result of physiological or behavioral adaptation [35]. The emergence and spread of resistance to the main insecticides could compromise the effectiveness of the preventive measures, operational implementation of control programs, and outbreak management.

1.4. Mechanisms of insecticide resistance

There are three major categories of insecticide resistance that have been described, namely, physiological resistance (target-site resistance and metabolic resistance) and behavioral avoidance. First, physiological resistance may develop due to the target-site resistance. Target site mutations are known to cause amino acid substitutions, which could affect the influx of insecticides into the target site. This may compromise the action of the insecticide rendering the vector tolerant or fully resistant to the insecticide. Another form of physiological resistance is due to metabolic resistance due to detoxification of insecticides by cytochrome P450 monooxygenases which allow the resistant vector to metabolize insecticides [36]. Glutathione S-transferases (GSTs) and carboxylesterases (ESTs) are also described in this process. Over expression of P450s was associated with insecticide resistance in diverse vector species including *Ae. aegypti* [37]. The resistant vectors accumulate high levels of efficient enzymes that detoxify the toxins. The second mechanism of resistance is known as behavioral adaptation or avoidance of the vector, this is well characterized in *Anopheles* mosquitoes. Therefore, monitoring insecticide resistance is crucial in the implementation of vector control strategies.

1.4.1. Physiological resistance in Aedes spp.

In Tanzania, like many other African settings, there is limited information on the *Ae. aegypti* resistance, most of the resistance data were collected mainly in the Americas and Asia. Our recent study in Dar es Salaam [24] demonstrated that the majority of *Ae. aegypti* strains were resistant to pyrethroid class of insecticide; mortality ranging from 83 to 92% in Dar es Salaam City. Data on molecular markers of resistance are scarce; however, studies elsewhere have correlated the occurrence of the knockdown resistance (kdr) mutations and resistance to pyrethroid and DDT [29, 34, 37, 38].

The mechanism of action of the pyrethroid compounds is through their toxic effect and subsequent disruption of the VGS channels in the insect nervous system [32]. The evidence suggests that *Ae. aegypti* resistance to pyrethroids is conferred by the *kdr* mutations in the VGS channel [29, 39]. Nonsynonymous mutations in *kdr* gene are associated with insecticide resistance to DDT and pyrethroids on codon V1016I and F1534C in domains II and III of the VSG channel in *Aedes* spp. [40]. Other studies demonstrated the role of *kdr* gene mutation I1011M/V and F1269C in association with *Ae. aegypti* resistance [33, 34, 41]. In African settings, the occurrence of F1534C in concurrence with the V1016I mutation was also observed in Ghanaian *Ae. aegypti* population [42]. The more recent study demonstrated the significant role of *kdr* mutation V410L alone or in combination with the F1534C in reducing the sensitivity of *Ae. aegypti* to both type I (e.g., permethrin) and type II (e.g., deltamethrin) pyrethroids [32].

In addition to the *kdr* mutations, metabolic resistance is also know to lead to a physiological resistance due to the increase in the synthesis of detoxifying enzymes or in their specificity to metabolize the insecticide, both resulting in an enhancement of the insect detoxifying capacity of the vector [43, 44]. The P450 monooxygenases were shown to play a significant role in modulating resistance as revealed by high-throughput assays, by comparing the overall profile at genomic and transcriptome levels between resistant and susceptible populations [37]. A study that characterized several P450s, four CYP's, 9 J32, 9 J24, 9 J26, and 9 J28, conferring insecticide resistance in *Ae. aegypti* [37]. The CYPs were shown to be capable of metabolizing deltamethrin and permethrin; two common pyrethroid-based insecticides are widely used in vector interventions. Furthermore, there is evidence on the role of glutathione transferase (GST) enzymes in conferring resistance to several classes of insecticides [45]. In *Ae. aegypti*, the GST occurs as a cluster of genes in chromosome 2 and is shown to play a significant role in the metabolism of DDT [46]. Over expression of the GST enzyme is associated with DDT and pyrethroid resistant in *Ae. aegypti* populations. We, therefore, characterized additional members of this class in *Ae. aegypti* and provide evidence for a role of two additional GSTs in conferring resistance to insecticides.

1.4.2. Behavioral resistance in Aedes spp.

Thus is defined as the ability of a vector to detect and escape from an insecticide-treated area and avoid the toxin. This type of resistance has been shown in different classes of insecticides, including organochlorines, organophosphates, carbamates, and pyrethroids [47]. It has been shown that vectors are capable of avoiding feeding if they come across certain insecticides or escape the area sprayed with the insecticides. There are currently limited studies exploring this mechanism of resistance in *Ae. aegypti.* This paucity of information could hamper control programs since insecticide resistance could spread and render the insecticides ineffective. Therefore, more studies to assess the current susceptibility status of insecticides used for vector control are needed to describe the status to support control strategies.

2. Disease transmission by *Aedes aegypti*

Ae. aegypti mosquito is a major vector of dengue virus represented by four closely related serotypes called dengue 1, 2, 3, and 4 cause different illness including dengue fever, dengue shock syndrome, and dengue haemorrhagic fever. Dengue virus (DENV) belonging to the family Flaviviridae and genus *Flavivirus* [48].

Transmission of dengue fever (DF) occurs when a female *Aedes* spp. mosquito obtains its blood meal from an infected person during the period of viraemia. Mosquito-borne viruses multiply in both invertebrate and vertebrate cells where they cause cytopathic effects and cell destruction. Vector mosquitoes become infected when they feed on blood of a viremic vertebrate host in which there are sufficient circulating viral particles to provide an infectious dose to the mosquito.

A mosquito with salivary gland infection may transmit infectious virions during salivation as it probes the tissues of another vertebrate host. Transovarial transmission of virions occurs from the female mosquito to her progeny, and females of the next generation can transmit the virus orally without having been infected through blood feeding. There is also a venereal transmission of some arboviruses from male to female mosquito as observed and reported by Amarasinghe and others [49] (**Figure 2**).

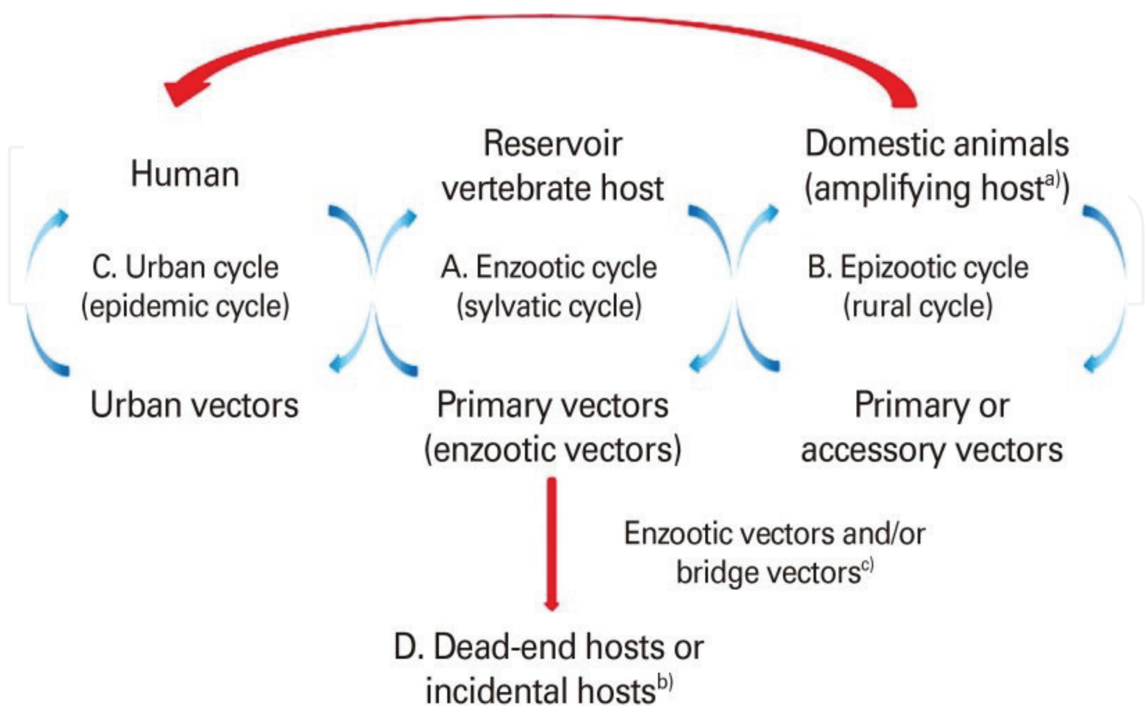

Figure 2. Arboviral transmission cycle vectored by *Aedes* mosquitoes.

Transmission of dengue virus occurs in 3 cycle, namely, enzootic cycle, epizootic cycle, and epidemic cycle. The enzootic cycle involves monkey-Aedes-monkey cycle, and this cycle is primitive and has been reported in South Asia and Africa [50]. The second is epizootic cycle, which involves the transmission of dengue virus from nonhuman primates to the next human in epidemic cycles by Aedes mosquito. Lastly, the epidemic cycle where the transmission cycle is through human *Ae. aegypti* contact, human cycle with periodic, or cyclical epidemic (**Figure 2**).

In this life cycle (human-to-*Ae. aegypti* mosquito-to-human cycle), the main dengue virus transmission is through mosquito that usually acquires the virus after feeding on the blood of an infected person. Replication of the virus occurs in the epithelial lining of the mosquito's midgut and then the virus move to haemocoele to infect the salivary glands. The virus can be transmitted though saliva during probing or blood feeding. The extrinsic incubation period may take 8–12 days, and this mosquito remains infected in all her life [50].

Infected humans are the major carriers of the virus where mosquito can acquire the virus through biting. The incubation time varies from virus to virus, but generally, arboviruses exhibit between 2–15 days from inoculation to development of clinical symptoms. During this period, *Aedes* mosquito can acquire the virus after feeding this person.

The reemergence of dengue disease in other places may be associated with the transovarial (via the eggs) transmission of dengue virus by *Ae. aegypti.* Dengue fever cannot spread directly from one person to another. Usually, *Ae. aegypti* prefers to feed mammalian hosts and will like to feed on humans, and even in the presence of other hosts (anthropophilic behavior), this behavior together with multiple feeding habit and highly domesticated behavior can make it an efficient vector.

3. Seasonality and intensity of transmission

Usually, dengue transmission occurs in rainy seasons with appropriate temperature and humidity for surviving of adult and larva mosquito. On the other hand, in arid areas, the rainfall is scant, and therefore, during the dry season, the man-made containers become the main breeding sites for the *Aedes* mosquito. Therefore, this can increase disease transmission.

In the ambient temperature, the life cycle of *Aedes* is shortening; also, there is production of small size mosquitoes, which may lead to the reduction of extrinsic incubation period. This small size mosquito may take more blood meal for egg production, which may lead to the increase in the number of infected mosquito and speedup the disease epidemic in the next dry season [50–52].

Several entomological factors have been associated with the initiation and maintenance of the epidemic including behavior, density, and vectorial capacity of mosquito vector population and introduction of the virus into a community.

4. Control and surveillance

4.1. Community education

This can be done by professionals by giving the public awareness, which can help to empower people to take control of mosquito breedings around their surroundings and adult control. The public can be provided with the tools needed to reduce mosquito annoyance. This is when the community, families, and individuals involved in planning and implementation of local vector control activities in order to ensure that the program meets priorities and the needs of the people in the community.

4.2. Larval mosquito control

Frequent larval breeding sites should be searched and treated as frequent as possible by trained field technicians and trained community members. Mosquito elimination in larval stages before emerging to adults will reduce the adult mosquito population. Reduction of mosquito breeding sites such as jars, barrels, pots, vases, bottles, tins, water coolers, and tyres can be done by environmental management, removing of solid waste and managing artificial man-made habitats. All domestic water storage containers should be cleaned and covered daily.

4.3. Adult control of *Aedes aegypti*

This should aim to control *Ae. aegypti* population. The use of insecticides such as lambda cyhalothrin- or deltamethrin-treated material by hanging them on windows and used as water jar covers may reduce *Ae. aegypti* population [53]. The use of insecticide space spraying, coils, and vaporizers in the community may reduce the mosquito population.

4.4. Use of repellents

Application of repellents such as DEET, DIMP, and of like is of paramount importance in reducing or controlling human to vector contact. The application should be done during active hours of the day.

4.5. Surveillance

Surveillance is important detect mosquito species in a certain area and changes in populations. By having valuable data, we are capable of more successfully time larvicide applications and more correctly target the adulticide activities. The WHO recommends of regular household surveys of *Aedes* spp. collecting evidence on the ecological and epidemiological indices to guide prevention and control strategies. This involves determining the habitat productivity, preference of the breeding sites, containers for the presence of egg, larvae and pupae as well as the collection of adult mosquitoes for further identification. Larval surveys involve identifying the presence of immature mosquitoes in breeding sites such as discarded tyres, containers, and water storage vases in the defined targeted area. Through this assessment, it is possible to identify most containers that are positive for *Aedes* spp. and parameters such Container Index (CI) and Breteau Index (BI) [6]. On the other hand, pupal survey is performed in houses and other breeding sites to identify the productivity in the breeding habitat [7]. In addition, surveys to determine the prevalence and circulating serotypes of DENV, ZIKV, CHIKV, and YFV as a part of regular surveillance are required to inform strategies to prevent transmission and provide early warning signal of outbreaks of clinical infections.

5. Discussion

Ae. aegypti remains a serious public health threat due to its importance in arboviral transmission, DENV, CHIKV, and ZIKV transmission. Globally, the incidence of DENV infections is on the rise, and recently, reemergence of CHIKV and ZIKV has been observed. Vaccine, prophylaxis, and therapeutics for most arboviral infections are still in development pipeline; hence, integrated vector management remains the cornerstone to stop outbreak transmission and sustainable control. Therefore, understanding of the ecology is important for outbreak prediction and effective planning of strategies to control transmission of arboviral infections.

Studies on the ecology of *Ae. aegypti* are important to better understand the preference of the vector in terms of the oviposition and colonization of mosquitoes [8]. The ecological factors play a role on influencing the population dynamics of larvae and pupae. The evidence is clear that both abiotic and biotic factors are important determinants of adulthood characteristics of life cycle such as longevity, fecundity, and body size [8, 9]. The factors are important to explain the vectorial capacity of *Ae. aegypti* on disease transmission. Furthermore, there is compelling evidence that *Ae. aegypti* is most productive in containers, which varies among regions, geographical settings, and seasonality [10]. In addition, it undoubtedly clears that water storage containers and discarded containers influence the vector density and risk of arboviral transmission particularly in poorly planned cities in (sub-)tropical regions [11]. Unless appropriate actions are taken, increasing urbanization, poor environmental management will continue to influence the stability of the *Ae. aegypti* populations. In addition, the vector density is influenced significantly by environment factors and urbanization [9, 11, 13]. *Ae. aegypti* feed exclusively on human and is increasingly a threat particularly in unplanned (peri-)urban areas. The recent data highlight the increasing *Aedes* spp. abundance and urbanization that could potentially escalate the risk of arboviral outbreaks [31]. Furthermore, the environment contributes to the breeding and ecological colonization of the vector. The presence of organic nutrients and microorganisms such as cyanobacteria seems to have influence on the productivity and development of *Ae. aegypti* [11, 15]. The presence of microalgae in the larval habitats, therefore, represents high adequacy of nutrients for immature stages of *Ae. aegypti* [11, 15]. Microalgae are associated with the presence and abundance of the vectors being the source of food for the larvae in breeding habitats. The evidence suggests that better understanding of these factors may be a useful indicator for mosquito population control. Measures to control microalgae to deprive nutrients to the vector could be explored for additional measures of the vector control. Importantly, approaches targeting immature stages of *Ae. aegypti* are highly recommended for effective and sustainable vector control. *Ae. aegypti* vector lays eggs in containers, buckets, care tyres and water storage vases; thus, the appropriate intervention such as proper disposal and management of containers and discarded tyres for source reduction could prove effective in reducing the vector population and mitigate the risk of arboviral transmission. Therefore, implementation of strategies to address the challenge of reemergence and expansion of arboviral infections will require a strong multisector commitment and integration for effective surveillance and control at regional, national, and program levels.

There is widespread resistance to the commonly widely used insecticide, pyrethroids and organophosphates in *Aedes* spp. control. Insecticide resistance is likely to impact disease outbreak and transmission measures and cost of the interventions [16, 17]. This is currently a major concern in South America where organophosphates, pyrethroids, and DDT have been widely used in vector control. However, there is also evidence on decreased susceptibility to pyrethroids in Sub-Saharan Africa and Asia [10, 13]. The origin and evolution of *Aedes* spp. resistance to insecticides remain unclear; however, it is assumed that the use of the insecticide in other vector interventions such as malaria control and agricultural may have exerted selective pressure on the *Aedes* spp. The mechanism of *Ae. aegypti* resistance to insecticides seems to be mediated by the nonsynonymous mutations *kdr* gene [18, 19]. Other studies suggest the role of enhanced enzymatic biodegradation or sequestration [20, 21]. Studies suggest the potential role of the metabolic enzymes including cytochrome P450s and GSTs in conferring resistance to pyrethroids and organophosphates in *Aedes* spp. Evidence on the possible behavioral resistance or avoidance is patchy, and more investigation is needed to understand how it may affect the current interventions. Despite the worsening *Ae. aegypti* resistance to pyrethroids and organophosphates, studies on susceptibility profile of *Bti* are reassuring that *Aedes* spp. retains considerable susceptibility to the biolarvicides [17]. Therefore, *Bti* remains a suitable alternative for prevention and control tool in regions where resistance to pyrethroids is widespread. To mitigate the risk of resistance and its public health consequences, it is crucial to strengthen monitoring and surveillance at all levels. Susceptibility testing of the commonly used insecticides and biolarvicides using the standardized WHO bioassay protocol should be integrated as part of the surveillance program and profiling of molecular markers of resistance may be considered as appropriate.

6. Conclusion

Aedes aegypti is the most important vector in outbreak and transmission of arboviral infections. The environmental factors favor mosquitoes and risk of disease transmission. The diseases are expanding particularly in (sub-)urban settings with frequent water shortage, high human population, poor planning, and poor waste disposal systems. Primary prevention and control measures are to reduce the vector exposure, but current vector control tools are unsustainable and there is increasing threat due to insecticide resistance. Integration of *Aedes* spp. vector control with other ongoing program and coordination of insecticide resistance monitoring and management is crucial to increase the impact of interventions. Future interventions will require deployment of effective vaccines against arboviral infections combined with integrated vector management.

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