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Review

Insecticide Resistance in *Aedes* Vectors of Arboviruses, Review

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Abstract

***Aedes aegyti* and *Ae. Albopictus* are major vectors of arboviruses such as Chikungunya virus, dengue virus, Rift Valley fever virus, yellow fever virus, and Zika virus. Vector control of *Aedes* using insecticides is important in the control of the transmission of these viruses to humans but these efforts are threatened globally by the emergence of insecticide resistance. This review focuses on cases of insecticide resistance in *Aedes* to the four classes of insecticides approved by World Health Organisation (WHO) for vector control. Studies show that *Aedes aegypti* and *Aedes albapictus* have developed resistance to all the classes of insecticide in various locations. However, few studies in Pakistan showed that some areas *Aedes* are susceptible to Carbamate. Therefore, to avoid re-emergence of arbovirus epidemics, insecticide resistance should be continued to monitor. Once insecticide resistance is established in a population, there is a real danger of the re-emergence of vector-borne diseases that had been presumed to be under control. There is also an emergency demands for new active ingredients based on novel modes of action or insecticidal compounds acting on new binding sites in already established targets in order to diversify the means of the vector control and to prolonged the life span of all the available insecticides, thereby reducing the risk of insecticide resistance leading to re-emerging arbovirus diseases.**

Keywords: *Aedes, Aegypti, Albapictus*, Insecticide, Resistance

INTRODUCTION

Diseases associated to arboviruses such as Dengue, Chikungunya, Yellow fever, Rift valley fever and Zika viruses causing death and severe health condition leaving millions of people suffering with disability and life threatening situations. This is as a result of their vector insecticide resistance to the four major classes of insecticide (Organochloride, Organophosphate, Carbamate and Pyrethroid) approved by World Health Organization for vector control with many countries in Africa and Australia bearing the highest burden (Moyes *et al.,* 2017). *Aedes albopictus* and *Aedes Aegypti* are aggressive, daytime biting arboviruses vectors that are widely spread throughout the world and are public health threat, following their primary role in transmission of dengue virus (DENV) and Chikungunya virus (CHIKV) causing outbreaks in many countries of East Asia and Islands of the western Pacific and Indian ocean and colonized all continents except Antarctica in the past 30–40 years (Caminade, 2012).

First discovery of *Ae. Albopictus* in Africa was in 1989 when larvae were detected in the port city of Cape Town, South Africa, in used tires imported from Japan; the infestation was immediately controlled but later, it was recorded in Nigeria and dispersed to Cameroon, Equatorial Guinea, and Gabon and spread across all Africa (Paupy, 2009). The females *Aedes* are primarily endophagic feeds indoors and endophilic lives indoors day-biting vectors that feed preferentially on humans which they take multiple blood meals before producing an egg batch and creates the potential for a single infectious female to transmit the virus to more than one person (Scott *et al.,* 2000). The female vectors lays their egg in containers found in the peridomestic environment, and that is where the immature larvae and pupae develop, they are ubiquitous in populated areas of the urban settlement which have favored their presence and abundance (Focks and Alexander, 2006). The accumulation of plastics and tires provides further breeding sites and contributes to the increased density of *Aedes* population in urban area (Gratz, 2004). Insecticide-based interventions have efficiently controlled *Aedes* mosquito populations for several years, as a result of the reliance on a few active ingredients registered and used in public health. Resistance to all four classes of insecticides (organochlorines, organophosphates, carbamates and pyrethroids) has developed in *Ae. Aegypti* and there is mounting evidence that these resistance is compromising the success of control interventions (Ranson *et al.,* 2010).

Organochlorines

Aedes aegypti resistance to Organochlorine (DDT) has been reported in a study by Kamgang *et al.* (2017) in Yaoundé, the capital city of Cameroon shows that *Ae. Aegypti* and *Ae. Albopictus*re resistance to DDT and deltamethrin, loss of sensitivity was noticed to permethrin and bendiocarb, and fully susceptibility to malathion. In a previous study by (Ishak *et al.,* 2017) revealed that *Ae. Albopictus* was resistant to DDT suggesting that the specie have developed resistance to the insecticide classes in the past five years. However, a striking difference was observed with other insecticides with higher resistance such as in deltamethrin (type II), permethrin (type I). Many studies showed that agricultural practices such as cotton or vegetable culture may have an essential role in the selection for DDT and pyrethroid resistance, especially for the main malaria vector *Anopheles gambiae, aedes and culex* in Africa.

Organophosphate

Reports on mosquito colonies resistant to organophosphate, are scarce. Recently, Tikar *et al.* (2009) reported temephos-induced resistance in an *Ae. Aegypti* colony in India. Before this, very few reports on selected temephos resistant mosquitoes were published (Wirth and Georghiou, 1999; Rodriguez *et al.,* 2002). In a recent publication, Macoris *et al.* (2007) revealed that in 1999 some mosquito populations of *Ae. Aegypti* from cities of the Northeast region of Mexico were found resistant to malathion. Studies on field populations performed in 2003 by Da-Cunha *et al.* (2005) showed that *Ae. aegypti* were resistant to temephos. In other studies *Ae aegypti* populations showed resistant temephos and cross resistance to other insecticides such as fenthion, feniltrothion, deltamethrin and cypermethrin (Rodriguez *et al.,* 2002; Tikar *et al.,* 2009; Wirth and Georghiou, 1999). Spray programs with malathion have been active in some Latin American countries where *Ae. aegypti and Culex quinquefasciatus* say *(Diptera: Culicidae)* cohabitate, the latter species has developed higher resistance than the former (Rodrı´guez *et al.* 2000, Hamdan *et al.* 2005).

Pyrethroid

Pyrethroids such as permethrin, deltamethrin, resmethrin and sumithrin are commonly applied mosquito adulticides. In addition, bednets, curtains and other household items treated with pyrethroids for personal protection are seeing increased use (Zaim *et al.,* 2000). With the deployment of pyrethroid-treated materials for dengue vector control likely to become more widespread in the future (Kroeger *et al.,* 2006), the occurrence of resistance may become common in many populations worldwide, and monitoring will be crucial to ensuring vector control. Metabolic resistance and target site insensitivity are both major forms of pyrethroid resistance (Soderlund and Bloomquist, 1990; Soderlund, 1997; Soderlund and Knipple, 2003).

Pyrethroids are used to control and prevent adult mosquitoes by ultra-low volume sprays, thermal fogging, pyrethroid-impregnated nets, etc. However, many dengue endemic areas are now facing the problem of pyrethroid resistance due to frequent and intensive use of these chemicals (Hemingway *et al.,* 2004). *Ae*. *aegypti* to pyrethroids has been reported from various countries in the understanding of the level and mechanism of resistance to the insecticides for developing appropriate vector control measures (Vontas *et al.,* 2012) Pyrethroids have been incorporated in the control program of *Ae. aegypti* in Venezuela only during the past 4 years, but earlier studies indicated that pyrethroid resistance was associated, in part, with resistance to DDT (Chadwick *et al*., 1977; Prasittisuk and Busvine, 1977). It is possible that the pyrethroid resistance we observed was a consequence of earlier exposure to DDT and./or recent applications of these insecticides. DDT use against *Ae. aegypti* in Venezuela was suspended in the early 1960s, but it is still being used for control of vectors of other endemic diseases such as malaria. In Singapore, pyrethroid resistance in *Aedes aegypti* due to an outbreak in 2005 where more than 14,000 Dengue fever cases were reported (Koh *et al.,* 2008). Piperonyl butoxide provide a well-established national vector control program that includes community engagement, law enforcement, and intersectional coordination, Since 2005, surveillance for dengue control has been based on four pillars: (1) case surveillance through mandatory notification of dengue cases to the Ministry of Health, by all medical practitioners; (2) vector surveillance through premises checks by vector control officers from National Environment Agency (NEA); (3) virus genotype surveillance at Environmental Health Institute of NEA; and (4) monitoring of other environmental parameters such as weather factors and population density. Clustering of cases and development of risk maps using the surveillance data allows prioritization of vector control operations (Komagata *et al.,* 2014).

Brengues *et al.* (2003) found pyrethroid resistance in *Ae. aegypti* strains from Semarang in Central Java, Belem in Brazil and Long Hoa in Vietnam. The highest level of resistance found at the Lethal Concentration (LC_{95}) occurred in the Semarang strain. Significantly, this was the strain in which resistant allele was found, suggesting that substitutions in the codon that confers knock down resistance. This study also found a number of individuals mosquitoes with the various mutations.

Carbamate

Ae. albopictus resistance to 0.1% bendiocarb (carbamate) with 83.50% to 92.07% mortalities range in a study conducted in Punjab. In similar study, *Aedes albopictus* collected from agricultural areas of Lahore, Sargodha and Faisalabad shows some level resistance to carbamates (Khan *et al.,* 2011). Resistance development in *Ae. albopictus* compared to *Ae. aegypti* may be due to its exophilic behavior, Although bendiocarb was found resistance in *Ae. aegypti* from Thailand (Intan *et al.,* 2015). *Ae. aegypti* population in five small towns surrounding the city of Merida, Mexico was found susceptible against bendiocarb while before Aedes albopictus collected from agricultural areas of Lahore, Sargodha and Faisalabad tested for resistance revealed high level of resistance to Organophosphates (Khan *et al.,* 2011).

CONCLUSION

Once insecticide resistance is established in a population, there is a real danger of the re-emergence of vector-borne diseases that had been presumed to be under control and by the time such resistance is detected, it is often far too late. The management of insecticide resistance or more precisely the management of arthropod pest susceptibility wherever possible – is crucial, and should be considered as one of the most challenging issues in modern applied entomology. This is especially true in the case of the effective management of malaria vectors. Controlling mosquitoes with only a limited number of chemical classes of insecticides is a challenge in itself, and, as outlined above, the chemical options for a resistance management strategy in adult mosquitoes are three (four if one includes DDT) chemical classes of insecticides addressing just two different target sites – a remarkably limited scenario. (Special larval treatments with insect growth regulators or bacterial endotoxins are also possible options, but larvae do not transmit diseases directly and they are often dispersed widely and difficult to locate.) The best strategy for to controlling disease vectors is the rotational use of insecticides of different modes of action altogether, rather than merely alternating members of one chemical class or different chemical classes that address the same target site (Nauen, 2007).

RECOMMENDATION

We recommend that, there is urgent need for new active ingredients to be incorporated into the existing insecticide that will alter the resistance mechanism of the vectors and will have a modes of action on new binding sites in the vectors and also extend the life cycle of the insecticides, thus lowering the risk of re-emerging vector-borne diseases

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