

Status of Resistant of Dengue, Yellow Fever, Chikungunya, Zika Vectors to different Insecticides in Eastern Mediterranean Region (EMRO) and Indian Subcontinent

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ARTICLE INFO

Received: 📅 April 09, 2021

Published: 📅 April 19, 2021

Citation: Hassan Vatandoost, Ahmad Ali Hanafi-Bojd, Fatemeh Nikpoor, Tahereh Sadat Asgarian. Status of Resistant of Dengue, Yellow Fever, Chikungunya, Zika Vectors to different Insecticides in Eastern Mediterranean Region (EMRO) and Indian Subcontinent. Biomed J Sci & Tech Res 35(2)-2021. BJSTR. MS.ID.005660.

Keywords: Resistant; Arboviruses; Insecticides; Eastern Mediterranean Region

ABSTRACT

Vector-borne diseases transmitted by insect vectors such as mosquitoes occur in over 100 countries and affect almost half of the world's population. Dengue is currently the deadliest arboviral disease but chikungunya and Zika show increasing prevalence and severity. Vector control, mainly by the use of insecticides, play a key role in disease prevention but the use of the same chemicals for more than 40 years, together with the dissemination of mosquitoes by human activities, resulted in the global spread of insecticide resistance. In this context, innovative tools and strategies for vector control are urgently needed. Arboviruses transmitted by mosquitoes represent a major health problem in EMRO countries. The main vector control activities include larviciding, space spraying, impregnated bednet and indoor residual spraying. The susceptibility status of the two main vectors of Arboviruses, *Aedes aegypti* and *Ae. albopictus* was evaluated in different regions of EMRO and Indian subcontinent.

Resistance to different insecticide classes such as pyrethroids, organophosphate, organochlorine, carbamates used as imogicide and larvicide were evaluated using WHO guidelines. An intensive search of scientific literature was done in "PubMed", "Web of Knowledge", "Scopus", "Google Scholar", "SID", etc. Results showed a wide variety of susceptibility/resistance status to these chemicals according to the location. Historical context of pesticide used, genetic background of vectors, age and abdominal conditions of adults may play a role in the susceptibility status of these species to different insecticides. Monitoring and mapping of resistance in countries should be carried out for appropriate vector control.

Introduction

Diseases transmitted by mosquitoes include malaria, dengue, West Nile virus, chikungunya, yellow fever, filariasis, tularemia, dirofilariasis, Japanese encephalitis, Saint Louis encephalitis, Western equine encephalitis, Eastern equine encephalitis, Venezuelan equine encephalitis, Ross River fever, Barmah Forest fever, La Crosse encephalitis, Zika fever, Keystone virus and Rift Valley fever: Usutu virus. Currently dengue is spreading worldwide,

placing at risk around 40% of the global population [1]. To date, no specific drugs are available and dengue treatment is restricted to supportive care. The major dengue vector is *Aedes aegypti* and *Aedes albopictus* which their distribution is shown in Figure 1. An estimated 50 million dengue infections occur annually and approximately 2.5 billion people live in dengue endemic countries. In addition, the recent chikungunya and Zika virus dispersion

throughout the globe. Actions against dengue are mostly focused on the reduction of mosquito densities, and vector control can be accomplished through mechanical, biological, and chemical approaches [2].

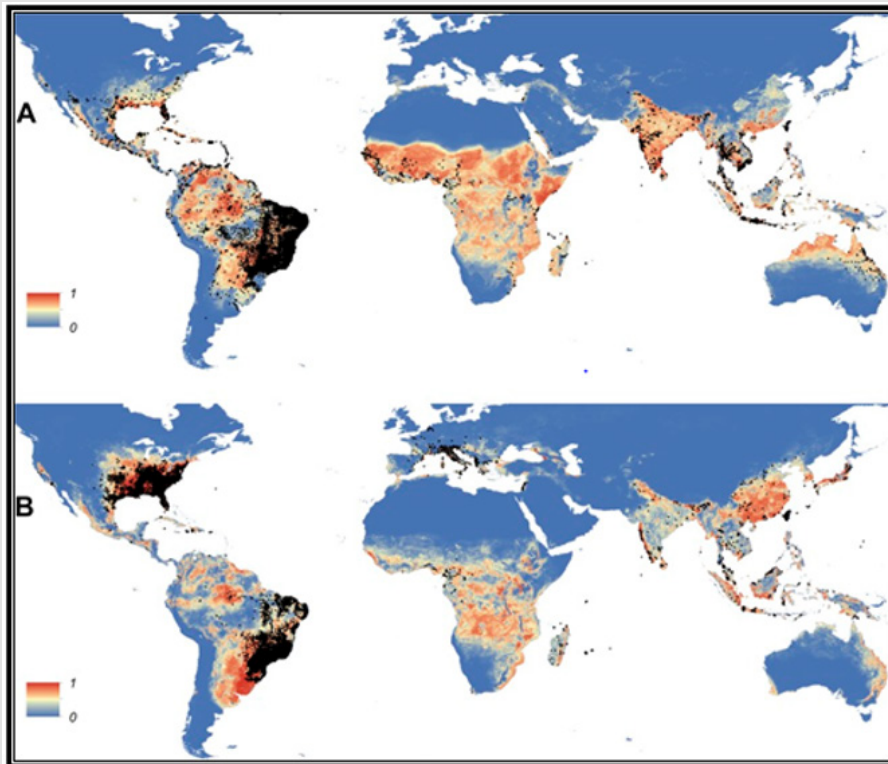


Figure 1: Global distribution of *Aedes aegypti* (A) and *Ae.albopictus* (B).

Dengue is the most rapidly spreading mosquito-borne viral disease in the world. In the last 50 years, incidence has increased 30-fold with increasing geographic expansion to new countries and, in the present decade, from urban to rural settings [3]. According to the WHO guideline several insecticides recommended for mosquito control [4]. Insecticide Resistance is recognized by the World Health Organization (WHO) as an important threat to arboviral disease control and prevention. There is an urgent need to identify the countries and regions where resistance could challenge vector control and to accelerate the deployment of innovative tools for vector control. Better understanding of the strength and dynamics of insecticide resistance will help to develop a global strategy for insecticide resistance containment in arbovirus vectors. Outbreaks of dengue have been documented in the Eastern Mediterranean Region possibly as early as 1799 in Egypt [5].

Recent outbreaks of suspected dengue have been recorded in Saudi Arabia, Sudan and Yemen, 2005-2006 [5,6]. Yemen is also affected by the increasing frequency and geographic spread of epidemic dengue in 2005. Since the first case of DHF died in Jeddah in 1993, Saudi Arabia has reported three major epidemics in 2011 [5]. The frequency of reported outbreaks continues to increase, with outbreaks for example in Sudan in 1985 [6] and in Djibouti in 1991 [7], and Somalia [8]. In 2015 an outbreak in Egypt that

occurred following a decade, long absence of reported cases from that country [9]. Pakistan may be represent the highest burden of dengue in EMRO region, since 2006, dengue epidemics have occurred every year and the range has extended to most cities in Pakistan. Dengue now affects thousands of people and has caused hundreds of deaths. It has become a major health problem in Pakistan, and it is likely to become an even greater health problem in the coming years [10].

On 1 May 2019, in response to increasing numbers of dengue fever cases in Pakistan and India, health authorities in Afghanistan heightened monitoring for the disease. The 14 cases were reported from six provinces. This is the first report of people with autochthonous, meaning locally acquired cases of dengue fever in Afghanistan. Both *Aedes albopictus* and *Aedes aegypti* are present in Afghanistan.

Results and discussion

All the results were followed as defined by WHO (1981, 1992, 1998) (11-13): susceptible when mortality was 98% or higher, possible resistant when mortality was between 97 and 90%, and resistant when the mortality was lower than 90%. An excel sheet was created for insecticide resistance based on the applied insecticide at diagnostic dosage recommended by WHO.

Deltamethrin and cypermethrin were used to evaluate resistance/susceptible status of field collected adult females of *Aedes aegypti* from Slum area of Misri Shah Lahore (Pakistan), the result indicated that *Aedes* females were more resistant to deltamethrin as compared to cypermethrin [11-14]. In Pakistan the results showed varying degrees of resistance in field populations. Resistance in *Ae. albopictus* to chlorpyrifos was generally very high while moderate to high levels of resistance were found with organophosphate, pyrethroid, new chemicals and two from carbamates [15].

In 2010 in Lahor resistance status of *Aedes aegypti* was evaluated against pyrethroid insecticide. Results indicated that *Ae. aegypti* field collected population from Government Islamia College for Women Cooper Road, Lahore was resistant to Deltamethrin. However, field population of *Ae. aegypti* from Government College University, Lahore was found susceptible [16]. In Sonitpur district of Assam insecticide susceptibility assays were performed on wild-caught adult female *Aedes albopictus* mosquitoes. *Ae. albopictus* was resistant to DDT (4%) in all study sites except Gohpur. The species was found to be 100% susceptible to deltamethrin (0.05%) in all study sites [17]. A survey was performed in Delhi on *Aedes albopictus*, Gurgaon (Haryana), Hardwar (Uttarakhand), Guwahati (Assam) and Kottayam (Kerala). Results revealed High resistance against DDT in Uttarakhand and Haryana population, whereas Delhi, Kerala and Assam populations showed tolerance.

Delhi population showed 97% mortality for deltamethrin and Kerala population showed 96% mortality against permethrin. All other populations studied were fully susceptible against both pyrethroids [18]. The status of resistance in *Ae. aegypti* from Lahore (Pakistan) was evaluated against pyrethroids insecticide. Results indicated that *Aedes aegypti* field population from Government Islamia College for Women Cooper Road, Lahore (GICW) was resistant to Bifenthrin. Whereas the field collected population of *Ae. aegypti* from Government College University, Lahore (GCU) was found susceptible as compared to laboratory reared population [19]. A survey in Asam (India) showed that both *St.albopictus* and *St.aegypti* were fully resistant to DDT in all the study locations. Both the species were completely susceptible to deltamethrin and malathion except for *St. albopictus* at Sotia which displayed low level of resistance to malathion [20]. The result of insecticide susceptibility tests in Delhi (India) shows high resistance against DDT and moderate level of resistance to pyrethroids (deltamethrin; permethrin mortalities) [21].

The survey in Delhi revealed that adult *Ae. aegypti* was resistant to DDT and dieldrin, tolerant to propoxur and fenitrothion, but was susceptible to malathion, deltamethrin, permethrin and lambda-cyhalothrin. However, the larvae were found to be susceptible to all the three larvicides tested, viz. temephos, fenitrothion and malathion [22]. In the Jazan Region of Saudi Arabia adults *Ae.*

aegypti mosquitoes were found to be susceptible only to Cyfluthrin, whereas variable resistances were observed from Lambda-cyhalothrin, Deltamethrin, Permethrin, Fenitrothion, Bendiocarb and DDT insecticides. The *Ae. aegypti* larvae were resistant to Temephos and showed high susceptibility to Methoprene than Diflubenzuron. The larvae were more susceptible to Methoprene than Diflubenzuron [23]. In Port Sudan City, *Ae. aegypti* were found to be susceptible to Deltamethrin, Bendiocarb, tolerant to Lambda-cyhalothrin and resistant to DDT and Malathion [24].

A study in Republic of Yemen revealed that the mosquito larvae of *Ae. aegypti* were more susceptible to the OP insecticides sumithion than acifon, actellic and of onac respectively, while the pyrethroids fendona was more effective against larvae than aralin. Data indicated that adult mosquitoes of the field strain *Ae. aegypti* were resistant to the insecticides lambda-cyhalothrin, malathion and fenitrothion but were tolerant to deltamethrin, permethrin and cyfluthrin [25]. The few insecticide resistance data available revealed widespread resistance to DDT in *Ae. aegypti* across the country while resistance to organophosphates appeared more frequent in southern India. Pyrethroid resistance in *Ae. aegypti* and *Ae. albopictus* was reported in Delhi and Kerala regions [26-29]. Challenges for the control of arboviral diseases in India include the development of vector surveillance and resistance monitoring programs and the implementation of rational vector control strategies throughout the country.

There are several reports of resistant status and mechanism of insecticide resistance in *Ae. aegypti* and *Ae. albopictus* to different groups of insecticides in the world [30-54]. WHO (2020) [55] recommended several measures for prevention and control of Dengue including: preventing mosquitoes from accessing egg-laying habitats by environmental management and modification; disposing of solid waste properly and removing artificial man-made habitats, covering, emptying and cleaning of domestic water storage containers on a weekly basis, applying appropriate insecticides to water storage outdoor containers; using of personal household protection such as window screens, long-sleeved clothes, insecticide treated materials, coils and vaporizers, improving community participation and mobilization for sustained vector control, applying insecticides as space spraying during outbreaks as one of the emergency vector-control measures, active monitoring and surveillance of vectors should be carried out to determine effectiveness of control interventions.

Conflict of Interest

The authors declare that there is no conflict of interest.

Acknowledgment

This research is supported by Ministry of Health and Medical Education under code number of NIMAD 982984.

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ISSN: 2574-1241

DOI: 10.26717/BJSTR.2021.35.005660

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