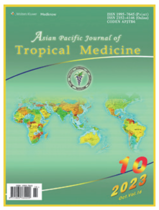

Review Article

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Insecticide resistance status of *Aedes aegypti* and *Aedes albopictus* in Malaysia (2010 to 2022): A review

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ABSTRACT

This review aimed to determine the prevalence of the insecticide resistance status of the field-collected *Aedes* (*Ae.*) *aegypti* and *Ae. albopictus* in Malaysia from 2010 to 2022 towards carbamates, organochlorines, organophosphates and pyrethroids. Biological and environmental controls were summarized with an emphasis on the mosquito vector control strategies in Malaysia. The information in this review was extracted from several databases such as PubMed (MEDLINE), Science Direct and Scopus by using keywords including "insecticide resistance", "carbamate resistance", "organochlorine resistance", "organophosphate resistance", "pyrethroid resistance", "*Aedes*" and "Malaysia", between January 2022 and December 2022. Distribution of resistant *Ae. aegypti* and *Ae. albopictus* in Malaysia was mapped using QGIS software. Insecticide resistance in both *Ae. aegypti* and *Ae. albopictus* is widespread in Malaysia, although the rates vary by states. The most notable was the steep increase in permethrin resistance of *Ae. aegypti* in Selangor, Malaysia, over the past decade. *Ae. albopictus* also displayed moderate resistance to permethrin, though not as widespread as *Ae. aegypti* in Selangor, but showed sign of resistance in Sarawak, East Malaysia. Resistance towards four main classes of insecticides have been widely documented in Malaysia. The extensive resistance towards permethrin in Malaysia which is one of the current insecticides used in Malaysia suggested that policies supporting the widespread use of permethrin fogging needs further evaluation.

KEYWORDS: *Aedes*; Pyrethroids; Insecticide resistance; Malaysia; Vector control

1. Introduction

Mosquitoes of medical importance, namely *Aedes* (*Ae.*) *aegypti* and *Ae. albopictus* transmit dengue, chikungunya, yellow fever, and zika

Significance

Increasing trend of resistance towards different types of insecticide is at an alarming rate. Resistance towards four classes of insecticide in *Aedes* population was well documented in Malaysia, especially towards permethrin and malathion. This study provides an insight of resistance status of *Aedes* mosquitoes in Malaysia, for a 12-year gap from 2010 to 2022. The report serves as a reference to local authorities and researchers for planning and monitoring the insecticide resistance status of mosquitoes in Malaysia.

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infection, which kill millions of humans every year[1]. In Malaysia, dengue fever was first reported in Penang in 1902 and dengue hemorrhagic fever has emerged in 1962 and since then, dengue cases have been reported regularly all over the country[2]. In the absence of effective vaccines and specific antiviral drugs, the strategies for preventing and controlling dengue rely solely on vector control intervention, primarily with the use of insecticides[3]. However, the excessive and long-term use of insecticides has led to resistance in mosquitoes. In Malaysia, evaluation of insecticide resistance status of *Ae. aegypti* and *Ae. albopictus* has been done in the stage of mosquito larva and adult using World Health Organization (WHO) and Centers for Disease Control and Prevention (CDC) bioassays[4,5]. Evidence of resistance towards all four classes of insecticides, *i.e.*, carbamates, organochlorines, organophosphates and pyrethroids have been reported in the population of the *Aedes* mosquitoes[4,6–8].

This study reports the distribution of insecticide resistance of *Ae. aegypti* and *Ae. albopictus* in Malaysia from 2010 to 2022, which would aid in monitoring resistance status and selection of the most appropriate insecticides used in vector control program.

2. Methodology

Literature was searched using online research databases including PubMed (MEDLINE), Science Direct and Scopus for articles on insecticide resistance of *Ae. aegypti* and *Ae. albopictus* in Malaysia using the following search terms: 'insecticide resistance' OR 'insecticide susceptible' OR 'pyrethroid resistance' OR 'organochlorine resistance' OR 'organophosphate resistance' OR 'carbamate resistance' AND '*Aedes*' AND 'Malaysia'. Information was screened, between January 2022 and October 2022, from all English-written publications and only articles documenting insecticide resistance based on WHO bioassay of field-collected *Ae. aegypti* and *Ae. albopictus* (adult and larval stage) in the year of 2010 to 2022 were included in this review. From the data gathered, 18 published paper were extracted and resistance of *Ae. aegypti* and *Ae. albopictus* in Malaysia were mapped using QGIS software (version 3.22.2) (Department of Land Affairs, Eastern Cape).

3. Mosquito vector control strategies in Malaysia

Vector control aims to disrupt transmission of mosquito-borne diseases and reduce the incidence of infection by shortening the longevity of immature and adult mosquitoes[9]. This can be achieved through chemical, biological and environmental approaches[10]. As dengue has become a notifiable disease in Malaysia since 1971, laws and legislations were introduced to regulate the prevention and control of vector-borne diseases, *e.g. Destruction of Disease–Bearing Insects Act 1975 (Act 154)*, *Prevention and Control of Infectious Diseases Act 1988 (Act 342)* and *Local Government Act 1976 (Act 171)*[11]. Additionally, Ministry of Health Malaysia (MOH) has implemented seven strategies in National Dengue Strategic Plan (2015-2020), which includes (Ⅰ) dengue surveillance, (Ⅱ) national cleanliness policy and integrated vector management, (Ⅲ) management of dengue cases, (Ⅳ) social mobilization and communication for dengue, (Ⅴ) dengue outbreak response, (Ⅵ) dengue research and (Ⅶ) reduction of dengue burden in Klang Valley[12].

3.1. Chemical control

Application of chemical insecticides for larviciding and adulticiding are the two significant mainstays of dengue vector control program. Nevertheless, one major drawback of prolonged chemical insecticide usage is the build-up of resistance in the mosquito population[13].

3.1.1. Chemical larvicides

Temephos (commercial name: Abate®) is one of the commonly used organophosphate larvicides. It can be used even in drinking water to kill *Aedes* mosquitoes in immature stage[14]. A new approach to control insects by using substances that can adversely affect insect growth development is known as an insect growth regulator (IGR)[15]. Beside being effective in controlling dengue vectors, IGR also possess low off-target toxicity and reduces risk to non-target organisms[16]. IGRs such as methoprene, pyriproxyfen, cyromazine and novaluron have been acting efficiently as a larvicidal agent when tested against *Aedes* population in Malaysia[17–19].

3.1.2. Space spraying

The chemical control of outdoor-biting adult mosquitoes in endemic area is carried out by space spraying using either ultra-low volume or thermal fogger[20]. Fogging is the most common control method of adult mosquito in Malaysia, however, it is primarily reserved for emergency situation. Starting from 1973, MOH requires healthcare practitioners to notify suspected cases of dengue to the ministry within 24 hours to initiate immediate fogging at affected areas[21]. House to house fogging will be carried out in the case house and 200 meters surrounding the case house for each case reported[22].

4. Biological control

Diverse biocontrol strategies cover engagement of a wide range of natural organisms that kill mosquitoes, exploiting mosquito behaviour to improve mosquito mortality, and releasing mosquitoes that are either sterile or unable to transmit diseases[23].

4.1. Elephant mosquitoes

Employment of *Toxorhynchites* mosquito is one of the efficient strategies as they feed on the larva of other mosquitoes and nektonic prey[24]. In Malaysia, Subang Jaya Municipal Council was among the first local authorities to use *Toxorhynchites* mosquitoes to control *Aedes* mosquitoes which resulted to a significant decrease in dengue cases in the area in 2014[25].

4.2. Bacillus thuringiensis israelensis (Bti) and Wolbachia bacteria

The use of bacteria as a tool for mosquito control such as *Bacillus thuringiensis israelensis* (Bti) has gained more popularity as it releases insecticidal toxins and virulence factors that selectively target the larval stage of insects[26]. Other than Bti, *Wolbachia* which is best known for its profound effects on host reproduction has been used to control dengue by introducing it into *Ae. aegypti* mosquitoes[27]. The mating between males and females that carry different and incompatible strains of *Wolbachia* will eventually reduce mosquito fecundity and egg hatching rate[28]. The *w*AlbB strain of *Wolbachia* has been successfully deployed for dengue control in dengue-endemic areas of Kuala Lumpur, Malaysia where decrement in dengue cases was observed in the released sites[29].

5. Environmental control

Uncontrolled and abundance of man-made containers in urban environment have promoted breeding of mosquito and enhanced disease transmission which contributed to the high rate of dengue cases in this country[30]. With the goal of destroying and controlling any disease-bearing insects, *Destruction of Disease–Bearing Insects Act* has been in effect since 1982[31]. During a house inspection, the house or premise owner will be issued a warning notice or a compound if found to breed *Aedes* mosquitoes and the owner is expected to abide by the instructions, otherwise court prosecutions will be proceeded[11].

6. Classes of chemical insecticides

Four major classes of chemical insecticides have been frequently used to control dengue vectors worldwide, namely organochlorines, organophosphates, carbamates, and pyrethroids[32].

6.1. Carbamates

Carbamates derived from carbamic acid, are widely used in household, gardening and agriculture as insecticides, fungicides, herbicides and nematocides[33]. Carbamates share a similar mode of action to organophosphates by inhibition of cholinesterase enzymes. However, the toxic action of carbamates is reversible, which makes it relatively less toxic than organophosphates[34]. In vector control, carbamates are used as an indoor-residual spray (IRS) in the form of bendiocarb, usually as rotation with pyrethroids[35].

6.2. Organochlorines

Organochlorines are chlorinated hydrocarbons developed in the 1940s and the most popular chlorinated insecticide of all time is known as dichlorodiphenyltrichloroethane (DDT)[36]. These compounds are known for their high toxicity, slow degradation and bioaccumulation but were mostly banned in developed countries due to chemical abuse[37]. Likewise in Malaysia, the regular application of DDT in IRS as vector control was undertaken after 26 years, which was then replaced with pyrethroids, such as deltamethrin in 1997[38].

6.3. Organophosphates

Organophosphates are considered less persistent in the environment than organochlorine, therefore it is still recommended by WHO for vector control[39]. In Malaysia, temephos (Abate® 1% sand granules) is recommended as a larvicide by MOH and has been widely used since 1973[19,40]. Traditionally, malathion was one of Malaysia’s chemical choices of dengue control. However, due to the unpleasant smell and oily residues left on the floor and wall of the building, the acceptance of fogging was low among the public and hence the use of malathion was stopped in 1996[41].

6.4. Pyrethroids

Since pyrethroids tend to be more potent, last longer in the environment and are less toxic to mammalian, they remain the most widely used insecticides, particularly in dengue-endemic countries[42,43]. Most household aerosol insecticides have active ingredients of either natural pyrethrin extract or synthetic pyrethroids (such as permethrin, deltamethrin, d-phenothrin, and prallethrin)[44]. In Malaysia, insecticides from the class of pyrethroids, namely permethrin and deltamethrin are used primarily for adulticiding purposes in the vector control program by the MOH[45]. Water-based pyrethroids (namely Resigen® and Aqua Resigen®) are used as an insecticide fogging formulation which have replaced malathion[41].

7. Insecticide resistance mechanism

According to WHO, insecticide resistance is defined as the ability of mosquitoes to survive exposure to a standard dose of insecticide, which may result from physiological or behavioral adaptation[46]. Frequent and long-term use of insecticide-based controls have contributed to the development of insecticide resistance, which challenges the current control of dengue. In mosquitoes, resistance is commonly associated with the target site and metabolic resistance[47]. The mechanisms of insecticide resistance in mosquitoes include reduced penetration of insecticides through the cuticle, metabolic resistance, target site resistance and behavioral avoidance[48].

7.1. Reduced penetration of insecticides

Reduced insecticide penetration is mainly caused by modifications of the insect cuticle where the cuticle becomes thicker, leading to slower rate of insecticide absorption and penetration, hence reducing the uptake of insecticide[49,50]. This mechanism of resistance has been studied by Ishak *et al*.[51], where the researchers observed highly over-expressed cuticular protein genes in permethrin resistant *Ae. albopictus* from Kuala Lumpur which suggests a strong association between the mechanism of reduced cuticle penetration and permethrin resistance.

7.2. Metabolic resistance

Metabolic resistance refers to the ability of the mosquito to detoxify insecticide before it reaches and binds to the target site[52]. Three families of metabolic enzyme are responsible for the metabolism of insecticide, namely esterases, glutathione transferases, and cytochrome P450s[53]. Among these enzymes, P450s are the primary family of enzyme associated with the resistance of pyrethroids[47] while glutathione transferases are usually associated with resistance of organochlorine DDT[54]. Metabolic resistance of pyrethroids is associated with up-regulation of cytochrome P450, particularly protein CYP6N3 and CYP6P12. Similar observation has been recorded in the *kdr*-free *Ae. albopictus* in Malaysia[51].

7.3. Target site resistance

Target site resistance of mosquitoes is inferred when the targeted site for insecticides is genetically modified or, altered thus limiting its interaction with neurotoxins and consequently eliminating the insecticidal effects[55]. The most important target site resistance for mosquitoes is *kdr* as it confers resistance to both pyrethroids and DDT. Four *kdr* mutations of F1534C, V1016G, S989P and A1007G have been detected in pyrethroid-resistant *Ae. aegypti* in Malaysia[42,45,56].

7.4. Behavioural adaptation

Any avoidance behaviour that results in an increased chance of survival for an insect or its offspring can be defined as behavioural resistance[57]. Mosquitoes can reduce or prevent negative consequences of insecticides through adaptation by either escaping from an insecticide-exposed environment upon physical contact or leaving the toxic area even before getting in contact with a treated surface[58].

8. Prevalence of insecticide resistance of *Aedes aegypti* and *Aedes albopictus* in Malaysia

The trend of insecticide resistance has increased over the past decade in which *Aedes* mosquitoes are becoming resistant to almost all the insecticides tested. The study of insecticide resistance status in Malaysia are mainly focused in urban areas such as Selangor and Kuala Lumpur. Overall, the effectiveness of pyrethroids towards *Ae. aegypti* were decreasing in time as multiple resistance towards this class of insecticide was reported[4,56,59]. Among the resistance trends, the most notable was the steep increase of pyrethroid resistance towards *Ae. aegypti* in Selangor[4,5,43]. Similarly, *Ae. albopictus* has gradually lost its susceptibility towards pyrethroids as resistant and incipient resistance towards pyrethroids was reported, though not widespread as in *Ae. aegypti*.

8.1. Carbamate resistance in Ae. aegypti

A study done from 2015 to 2016 has proven the effectiveness of propoxur in killing larvae of *Ae. aegypti* at concentration of

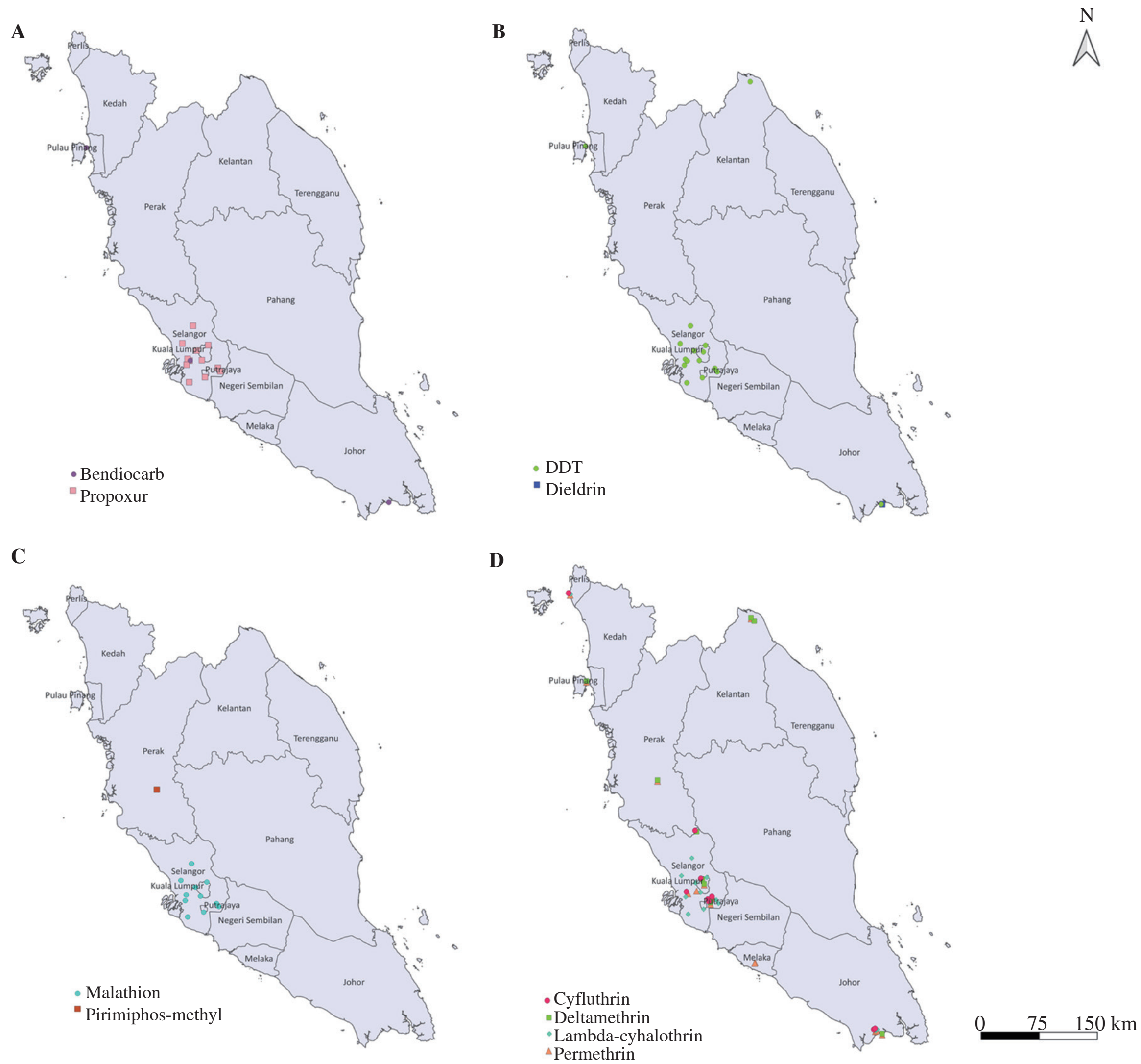

Figure 1. Distribution of resistant *Aedes aegypti* in Malaysia towards four classes of insecticide tested based on WHO adult bioassays from 2010 to 2022. The insecticides involved include (A) carbamates (*i.e.*, bendiocarb 0.1% and propoxur 0.1%), (B) organochlorines (*i.e.*, DDT 4 % and dieldrin 4%), (C) organophosphates (*i.e.*, malathion 0.8%, pirimiphos-methyl 0.25%) and (D) pyrethroids (*i.e.*, cyfluthrin 0.15%, deltamethrin 0.05% lambda-cyhalothrin 0.03% and permethrin 0.75%).

11.653 mg/L, causing a complete knockdown in WHO larval bioassay in all districts of Selangor[60]. While the larvae of *Ae. aegypti* were proven susceptible towards propoxur, the adults of *Ae. aegypti* of eight districts of Selangor state (namely Gombak, Hulu Langat, Hulu Selangor, Klang, Kuala Langat, Kuala Selangor, Petaling, Sepang) and Kuala Lumpur (sample collected from 2017 to 2018) were found to be highly resistants against propoxur 0.1% with mortality ranging from 0% to 28% in WHO adult bioassay (Figure 1A)[4]. In addition, adults of *Ae. aegypti* in Petaling district, Selangor state also has shown an evidence of resistance towards bendiocarb 0.1%[4,5].

8.2. Organochlorine resistance in Ae. aegypti

Larvae and adults of *Ae. aegypti* exhibits wide range of resistance level towards organochlorine insecticides. For example, larvae of *Ae. aegypti* from the districts of Selangor state (namely Klang, Kuala Langat, Sabak Banam and Sepang) were susceptible towards DDT 11.210 mg/L, recorded from 2015 to 2016, as more than 90% of mortality were recorded after being exposed for 24-hour in larval bioassay, except for the strains of Gombak district (88.44% of mortality) and Hulu Selangor district (32.95% of mortality)[60].

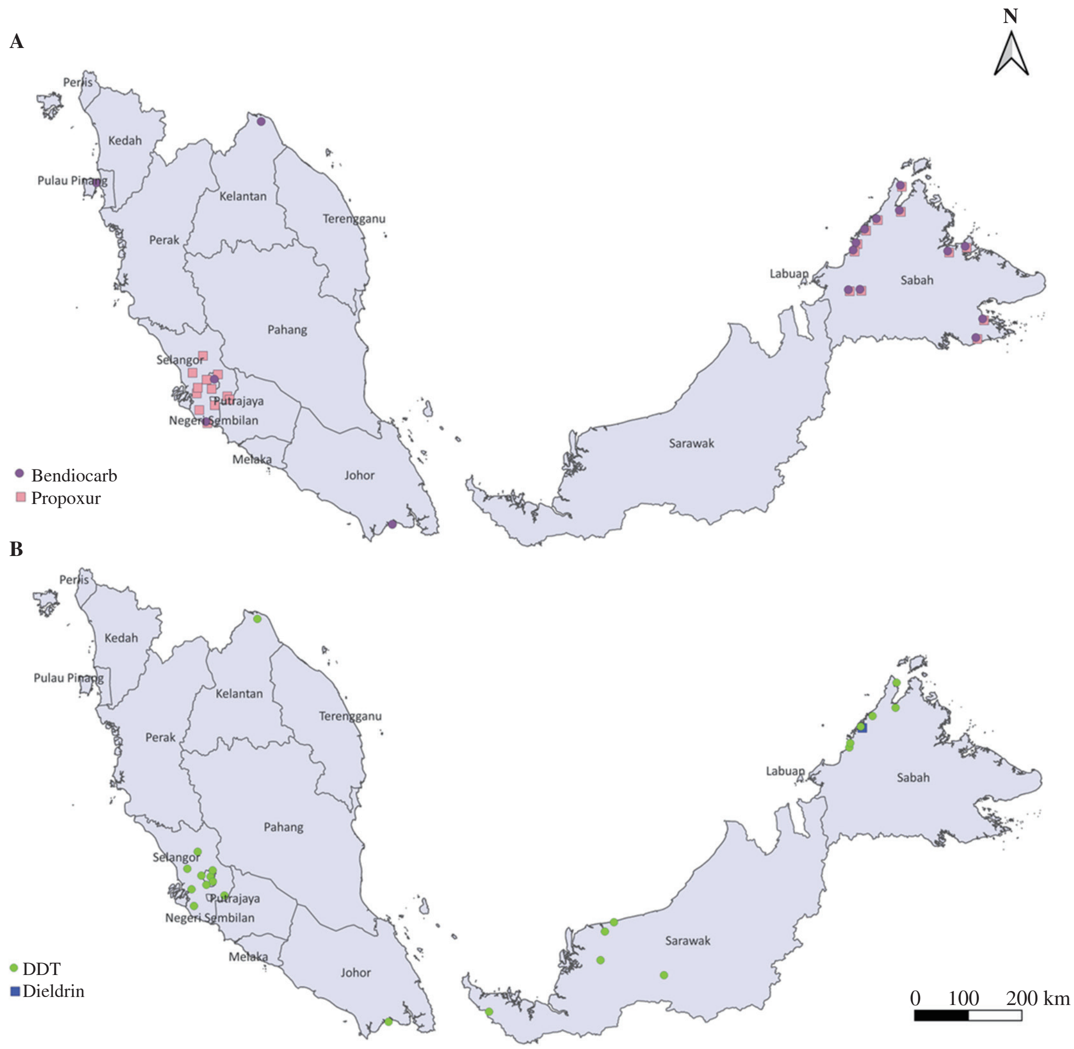

Figure 2. Distribution of resistant *Aedes albopictus* in Malaysia towards two classes of insecticide tested based on WHO adult bioassays from 2010 to 2022. The insecticides involved include (A) carbamates (*i.e.*, against bendiocarb 0.1% and propoxur 0.1%), and (B) organochlorines (*i.e.*, DDT 4%, dieldrin 0.4%).

However, when adults of *Ae. aegypti* were tested against the same insecticide from 2017 to 2018, high level of resistance towards DDT 4% was observed from the same districts[4].

Besides Selangor, resistance towards DDT 4% has also been documented in adults of *Ae. aegypti* from other states, namely Kuala Lumpur, Johor (Johor Bahru), Kelantan (Kota Bharu) and Penang since 2010. On the contrary, these strains were susceptible towards another member of organochlorines, which is dieldrin 4%, except for Johor Bahru strain (Figure 1B)[56]. The resistance towards DDT despite being banned for decades might be due to cross resistance towards pyrethroid as the insecticides share the same mode of action.

8.3. Organophosphate resistance in Ae. aegypti

According to a study published in 2018, temephos at concentration of 0.012 mg/L which was recommended by WHO as diagnostic dose for resistance monitoring program, has been reported to be ineffective to *Ae. aegypti* larvae collected from Kuala Lumpur and Selangor (Gombak and Hulu Langat) with mortality between 0% to 74% in bioassay[61]. Whereas, temephos at operational dosage of 1 mg/L was able to cause complete mortality to *Ae. aegypti* larvae which indicates temephos is still highly effective as a larvicidal agent[61].

Malathion at concentration of 0.629 mg/L has caused complete mortality in larvae of *Ae. aegypti* (susceptible) from 2015 to 2016 [60], resistance towards malathion 0.8% was observed in adult mosquitoes of *Ae. aegypti* in Kuala Lumpur and Selangor from 2017 to 2018 with mortality below 60%, even though the operation use of malathion in vector control program has been stopped for decades in Malaysia (Figure 1C)[4,41]. In contrast with a study published in 2018, *Ae.*

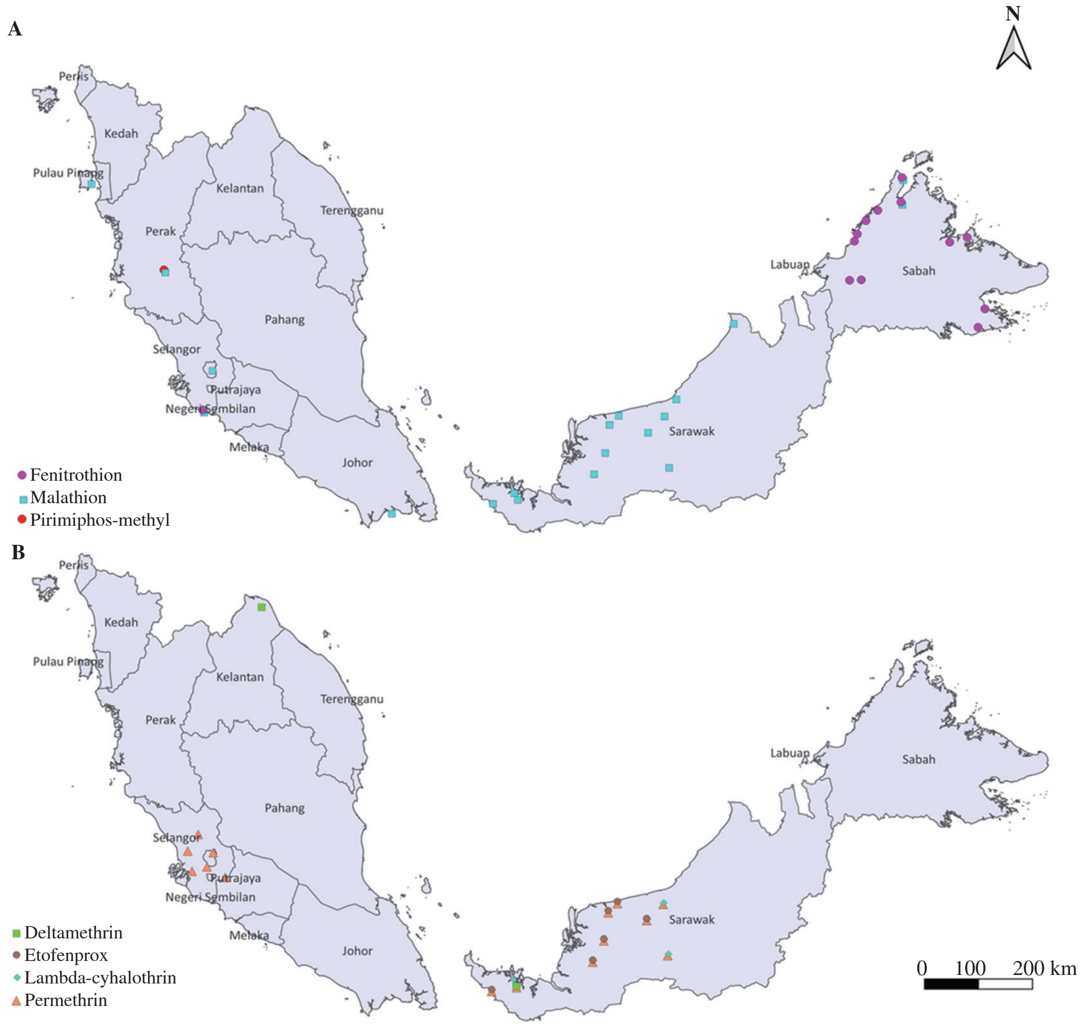

Figure 3. Distribution of resistant *Aedes albopictus* in Malaysia towards two classes of insecticide tested based on WHO adult bioassays from 2010 to 2022. The insecticides involved include (A) organophosphates (*i.e.*, fenitrothion 1.0%, malathion 5%, pirimiphos-methyl 0.25%) and (B) pyrethroids (*i.e.*, deltamethrin 0.05%, etofenprox 0.5%, lambda-cyhalothrin 0.05% and permethrin 0.25%).

aegypti strains of Johor Bahru and Perlis were fully susceptible towards malathion (0.8%) and fenitrothion (1%)[59].

8.4. Pyrethroid resistance in Ae. aegypti

From 2015 to 2016, larvae of *Ae. aegypti* has shown evidence of resistance towards cyfluthrin (0.003 mg/L), deltamethrin (0.03 mg/L), etofenprox (0.161 mg/L), lambda-cyhalothrin (0.022 mg/L) and permethrin (0.033 mg/L) in WHO larval bioassay in Kuala Selangor and Petaling district[60]. In the same period, adults of *Ae. aegypti* in Kuala Lumpur were fully susceptible to permethrin[30]. However, resistance towards permethrin 0.25% of the same strain was detected a year later[4]. Another dengue locality of urban areas in Malaysia, *Ae. aegypti* in Johor Bahru has been recorded to have resistance to all types of pyrethroids (*e.g.*, cyfluthrin, deltamethrin, lambda-cyhalothrin, and permethrin)[30,56,59], indicating that pyrethroid is no longer effective to be used as a vector control program in the state from 2010 to 2016. Selangor, which recorded the most dengue cases in Malaysia every year, exhibits a wide range of resistance towards the pyrethroid group. *Ae. aegypti* was resistant towards cyfluthrin, deltamethrin, lambda-cyhalothrin, and permethrin in Selangor except for the strain of Taman Sungai Jelok, Kajang, which was highly susceptible to cyfluthrin and deltamethrin as high percentage of mortality were recorded in WHO adult bioassay (100% and 99%, respectively)[30]. A study in 2017 provided additional evidence of resistance in Petaling district which suggests the resistance towards pyrethroids is serious in Selangor[62]. The resistance in the insecticide class of pyrethroids especially in dengue hot spot areas may be due to the frequent spraying of pyrethroids to reduce dengue vectors as dengue cases were continuously reported in these areas

(Figure 1D).

8.5. Carbamate resistance in Ae. albopictus

Widespread of resistance towards carbamates can be seen in Sabah state, as *Ae. albopictus* in all five divisions of Sabah state, namely Keningau, Kudat, Sandakan, Tawau and West Coast were resistant towards bendiocarb 0.1% and propoxur 0.1% with mortality of 47%-77% in WHO adult bioassay[8]. Additionally, propoxur 0.1% was not causing high mortality when tested against *Ae. albopictus* collected from Kuala Lumpur and eight districts of Selangor, indicating these mosquitoes were highly resistant towards the insecticide (Figure 2A) [4,63].

8.6. Organochlorine resistance in Ae. albopictus

A study performed at dengue-prone sites of Selangor and Kuala Lumpur from 2017 to 2018 documented resistance and incipient resistance of *Ae. albopictus* towards DDT 4% with mortality ranging from 27% to 97% in WHO adult bioassay[4]. Previously, field strain of *Ae. albopictus* in Kuala Langat, Selangor was fully susceptible towards DDT 4%[63].

Recent study done by Ali *et al*. revealed *Ae. albopictus* strain in the district of Kuala Langat had developed resistance where 61% of mortality towards DDT treatment was recorded (Figure 2B)[4]. Meanwhile, in Sabah, adults of *Ae. albopictus* in Beluran, Sandakan, Kunak, Tawau, Tenom, Keningau, Kota Kinabalu and Penampang were fully susceptible to DDT 4%, however the larvae of *Ae. albopictus* in the same districts were highly resistant to DDT (0.012 mg/L) as it did not cause any knockdown in WHO larval bioassay but was fully susceptible to another type of organophosphate, dieldrin (0.050 mg/L)[7,8]. Additionally, resistance towards DDT (4%) has been observed in adult mosquitoes collected from Bau, Sibu, Mukah, Dalat and Kapit, Sarawak[64].

8.7. Organophosphate resistance in Ae. albopictus

Increasing tolerance or resistance to different types of organophosphates can be seen in both larva and adult of *Ae. albopictus* in Sabah. The adult population of *Ae. albopictus* were resistant towards fenitrothion 1.0% from all study sites in the divisions of Keningau, Kudat, Sandakan, Tawau, and West Coast, Sabah state (Figure 3A)[8]. However, when larvae of *Ae. albopictus* were tested against the same insecticide (fenitrothion 0.02 mg/L) in WHO larval bioassay, high susceptibility was observed in the districts of West Coast division, which are Kota Belud, Papar and Tuaran[7].

In contrast, larva of *Ae. albopictus* exhibited strong resistance towards malathion (0.125 mg/L) with a complete absence of mortality but adults of *Ae. albopictus* collected from Kota Marudu, Kudat and Putatan districts were highly susceptible to malathion 5%[7]. On the other hand, malathion 0.8% resistance has persisted in field strains of *Ae. albopictus* collected from dengue-endemic areas of Kuala Lumpur and Selangor from 2017 to 2018[4]. A paper published in 2018 reported temephos resistance has been found in two divisions of Sabah; West Coast and Kudat with 0% to 27% of mortality in WHO adult bioassay[7]. In Penang, WHO larval bioassay revealed all collected strains of *Ae. albopictus* were highly susceptible towards temephos (0.012 mg/L and 1 mg/L) as complete mortality was observed according to a study published in 2016[65].

8.8. Pyrethroid resistance in Ae. albopictus

Pyrethroid is generally effective to be used as dengue management in East Malaysia, as study done in 2019 revealed *Ae. albopictus* found across 14 districts from the divisions of Kudat, West Coast, Interior, Tawau, and Sandakan of Sabah state were susceptible against cyfluthrin 0.15%, deltamethrin 0.05%, etofenprox 0.05%, lambda-cyhalothrin 0.05%, and permethrin 0.25%[8]. In contrast, latest study published in 2021 indicates that only cyfluthrin was able to induce 100% mortality in all tested strains in Sarawak state while incipient resistance and resistance toward lambda-cyhalothrin 0.05% was recorded (Figure 3B)[64].

In West Malaysia, resistance towards permethrin 0.75% has been detected in Kuala Lumpur strain in 2010[56]. Similarly, lambda-cyhalothrin 0.03% and permethrin 0.25% have failed to cause more than 90% of mortality in adults of *Ae. albopictus* from Kuala Lumpur, Gombak, Hulu Langat, Hulu Selangor and Kuala Selangor from 2017 to 2018[4]. In contrast with a study published in 2013, adult population of *Ae. albopictus* from Tanjung Sepat, Kuala Langat, Selangor was highly susceptible towards permethrin[63] but a recent study revealed the presence of permethrin (0.25%) resistance in *Ae. albopictus* of the same district-Kuala Langat from 2017 to 2018 (Figure 3B)[4].

9. Limitation

This review mainly focused on the resistance status determined by

WHO larval and adult bioassay, which are commonly used among researchers in Malaysia. Some of the reports are not standardized in terms of methods and approaches. The review is susceptible to selection bias, due to technical issue and availability of the resources.

10. Conclusions

Development of insecticide resistance can be seen in both *Ae. aegypti* and *Ae. albopictus* in Malaysia. To ensure the efficacy of vector control programs, insecticide resistance management programs need to be taken seriously to remain the insecticide susceptibility in *Aedes* vector. This includes implementing rotation, combination or mosaic resistance management strategies[66,67]. Continuous resistance monitoring should also be regularly conducted in all endemic dengue sites in Malaysia, to facilitate the selection of insecticides with the most significant promise for minimizing dengue infections.

Conflict of interest statement

The authors declare that they have no conflict of interest.

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Authors' contributions

All authors conceived and designed the research. SNN, KXY, MRS and WMAWN searched the literatures and analysed the data. SNN and KXY wrote the manuscript. AR, MNZ, TINTI and RD interpreted data and critically revised the manuscript. KXY supervised the project. All authors have read and approved the final manuscript.

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