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Insecticide resistance of *Aedes aegypti* in Indonesia: a systematic review

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ABSTRACT

In Indonesia, dengue hemorrhagic fever (DHF) continues to be an issue. Although there have been fewer dengue infections in the past three years, many areas of Indonesia remain dengue endemic. Insecticide use is one DHF prevention and control method that has been used for a long time. Long-term usage of insecticides can cause the vector, *Aedes aegypti*, to develop resistance. Insecticide resistance to *Aedes aegypti* in Indonesia was the focus of this study's analysis of the literature review. A systematic review using keywords based on population, interest and context (PICo) was employed in the study strategy. The databases used to find the publications were ScienceDirect, ProQuest, PubMed, Google Scholar, and Garuda from 2018 to 2022. Hence, 40 papers out of the 6,429 total articles were relevant and should be reviewed and analyzed. According to an analysis of the paper, it was discovered that *Aedes aegypti* mosquitoes are resistant to insecticides of the pyrethroid and organophosphate classes in various parts of Indonesia. However, it was discovered that several regions were both tolerant of and vulnerable to pyrethroids and organophosphates. If insecticides are to be utilized intolerant and vulnerable locations, monitoring and evaluation of their usage must be done, and a strategy of varying insecticide kinds and dosages and boosting community empowerment toward mosquito nest elimination behaviour must be implemented.

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1. INTRODUCTION

Dengue hemorrhagic fever (DHF) is an infection caused by the dengue virus, which is transmitted from *Aedes aegypti* and *Aedes albopictus* mosquitoes as primary vectors, as well as *Aedes polynesiensis*, *Aedes scutellaris* and *Aedes (Finlaya) niveus* as secondary vectors [1]. Over 50 years DHF in Indonesia has experienced an increase in cases, with an incidence rate in 1968 of 0.05 cases per 100,000 population to 22.55 cases per 100,000 population in 2017, with the highest peak incidence occurring in 1973, 1988, 1998, 2009 and 2016 [2]. The tendency of the most DHF cases often occurring from January to April can be attributed to meteorological factors, including rainfall and high humidity [3]. Over the past three years, there have been fewer DHF instances; from 2019 to 2021, there were 138,127 cases, down to 73,518 cases. Similarly, the number of fatalities brought on by DHF has dropped from 919 to 747. Between 2012 and 2020, Indonesia's case fatality rate (CFR) decreased from 0.9% to 0.69%. However, in 2021, this percentage will rise to 0.96%. The national policy for DHF control's aim of 0.7% is exceeded by the DHF case fatality rate [4].

Physical and biological management through initiatives to remove mosquito nests is the key tactic for limiting the DHF vector's ability to spread disease. Draining and sealing water reservoirs and burying discarded objects that might serve as mosquito breeding grounds are actions taken to eliminate mosquito nests. Many individuals think fogging is a better strategy to prevent DHF than removing mosquito nests, and many people need to know how important it is to do so [5]. Indonesia's North Sumatra Province utilized Malathion and Cypermethrin to control DHF, and it was reported that the vectors there were resistant [6]. West Sumatra reported that the *Aedes aegypti* population's genotype was resistant to Malathion and Permethrin [7]. Even though Wonosobo is a highland region, DHF transmission can still happen due to the high density of mosquitoes, which allows the Malathion-resistant mosquito population to continue to exist and breed [8]. Resistance to insecticides emerging Studies shows several mutations associated with pyrethroid resistance in *Aedes aegypti* collected from the city of Magelang; these mutations may be connected to the city of Magelang's modest population growth and human urbanization [9]. The non-specific increases in esterase and monooxygenase activity against *Aedes aegypti* are the basis for the resistance mechanism to Malathion and Cypermethrin [10].

Insecticides control mosquito populations since they can live when exposed to them, but repeated usage of an area may result in resistance [11]. Insecticides were formerly successful in keeping mosquitoes under control. However, the rise in DHF cases has led to an increase in resistance and a negative impact on the ecology and ecosystems, making insecticides useless [12]. Insecticides have been evaluated for their efficiency in combating mosquitoes, and strategies, including rotational application, which can prevent the emergence of resistance, have been suggested [13].

2. METHOD

The systematic review method was employed in this investigation. We used keywords based on the population, interest and context (PICo) categories. Five databases, including Science Direct, ProQuest, PubMed, Google Scholar, and Garuda, were searched for scholarly publications published between 2018 and 2022. All of the following keywords are utilized in each database: Indonesia AND *Aedes* OR dengue OR *aegypti* OR *albopictus* AND pesticides OR insecticide OR fogging OR organophosphate OR pyrethroid OR resistance OR knockdown OR mutation with year limit from 2018–2022. According to the screening findings, 39 articles satisfied the inclusion criteria and were relevant to the study issue (Figure 1).

For this systematic review, the several criteria were used to determine inclusion. The following requirements should be met: i) the article discusses insecticide resistance to larvae and mosquitoes of *Aedes aegypti* that occur in Indonesia; ii) the study should be a research article (descriptive, cross-sectional, case-control, cohort, or experiment); iii) it should have been published within the previous five years (2018-2022); and iv) open access, when the exclusion criteria were: i) non-Indonesian and non-English published studies; ii) publications that did not fit the topic of the study; iii) duplicate publications; and iv) incomplete text. Data analysis used descriptively includes reviewing articles, reducing data using a matrix of critical points from research articles, compiling data from the results of data reduction, presenting data, validating data using credibility tests, using reference materials in the form of theories discovered, and drawing conclusions.

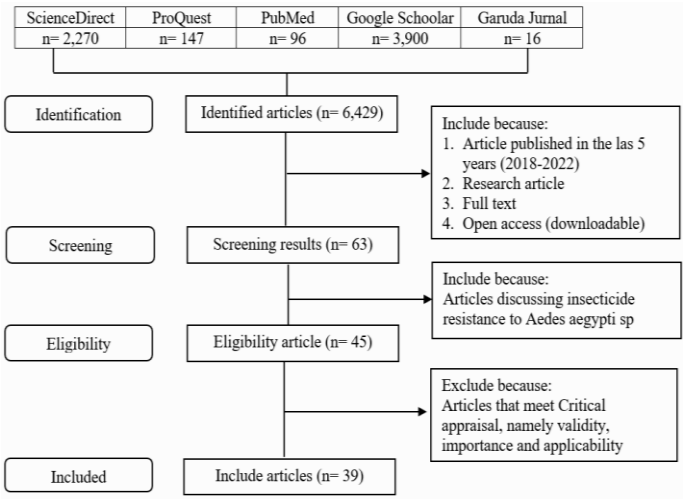

Figure 1. The search process on the article search engine

3. RESULTS AND DISCUSSION

Figure 1 reveals that there are 39 articles based on the results of a search engine literature search. The details of them [6], [14]-[50] are shown in Table 1 and Table 2 (see in Appendix). The article obtained examines the findings of insecticide resistance in mosquitoes and *Aedes aegypti sp.* larvae in Indonesia. There were 32 articles (82.05%) on the resistance of mosquitoes to pyrethroid and organophosphate class insecticides and seven articles (17.95%) on insecticide resistance to *Aedes aegypti sp.* larvae. *Aedes aegypti* mosquitoes have demonstrated organophosphate resistance in DHF endemic areas, namely 100% with the pesticide malathion 0.8% and a mosquito death rate of 80%, according to a study of studies from Indonesia. The pyrethroid organophosphate group, which includes cypermethrin, permethrin, and deltamethrin, is resistant to the *Aedes aegypti* mosquito in 98% of the resistant regions where DHF is prevalent. Urban regions where 0.2% and 0.5% cypermethrin pesticides are no longer effective. Additionally, it was discovered that most *Aedes aegypti* species in Central Java and the Yogyakarta Special Region were resistant to 0.05% lambda-cyhalothrin, 0.75% permethrin, 0.05% deltamethrin, and 0.5% etofenprox.

According to a published study collected in Indonesia, the *Aedes aegypti* mosquito has developed resistance to pesticides belonging to the organophosphate and pyrethroid families in dengue-endemic areas. Some groups that have experienced resistance include organophosphates, including malathion with a concentration of 5% and 0.8%, and the pyrethroid group, including alpha-cypermethrin with a concentration of 0.025%, deltamethrin with a concentration of 0.025%, and lambda-cyhalothrin with a concentration of 0.03%. The pyrethroid group is more resistant when measured against the overall mortality of *Aedes aegypti* mosquitoes based on article investigations of the two types of groupings.

3.1. *Aedes aegypti* mosquito resistance to organophosphate

Malathion can harm an insect's nervous system, such as a mosquito. Malathion permanently binds the cholinesterase enzyme in the nervous system of insects. Malathion is reportedly inexpensive, effective in halting the development of adult *Aedes aegypti* mosquitoes, economical, low-dose, and generally safe for humans [51]. It may also be used for thermal or cold fogging or fumigation. According to the research from the papers, some Indonesian provinces, including Sumatra, North Sulawesi, Bitung, Banyumas, Semarang, Bantul, and Sleman, are resistant to malathion. Mosquito resistance has been caused by exposure to malathion pesticides used in dengue control operations in Bitung Regency, and the general public utilizes domestic insecticides to prevent mosquito bites [34]. Malathion is used more often because fogging is preferred by users, allowing for frequent usage over a long period [16], [17]. The method for doing so on the -naphthyl acetate substrate increases non-specific esterase enzyme activity [27]. The voltage-gated sodium channel (VGSC) gene, which is linked to resistance to pyrethroid insecticides, is present. This is related to increased non-specific and non-specific esterase enzyme activity [33].

Because of metabolic detoxication enzymes, particularly esterases, *Aedes aegypti* is resistant to organophosphate pesticides. The active chemicals of insecticides that belong to the organophosphate family are synthetic and organic. Different kinds of organophosphate pesticides make up 30% of all insecticides. The primary mechanism of action of organophosphate insecticides is the suppression of acetylcholinesterase (AChE). AChE directs the hydrolysis of acetylcholine (ACh), which regulates hydrolysis in vesicles on axons near the synaptic cleft. After the impulse is transmitted, ACh and AChE hydrolyze into choline. In the absence of AChE, more ACh accumulates, disrupting impulse transmission, and causing decreased muscle coordination, convulsions, and eventual death. The electrophilic organophosphate substrate used by the AChE enzyme results in large quantities of ACh, which induce impaired motor coordination, convulsions, and, ultimately, death. However, it is vulnerable to insecticides because of a qualitative difference in esterases' capacity to hydrolyze *Aedes aegypti* more quickly than the *Aedes sp.* group. Two pathways that lead to resistance include excessive production and modifications in the catalytic properties of enzymes that are hypercatalectic to insecticides. Along with hydrolyzing the ester bonds, esterases also bind hard-to-hydrolyze organophosphates, such as those containing phosphate groups. Therefore, sequestration is not an ester hydrolysis resistance mechanism [52]. The chemical control plan must include ongoing monitoring of pesticide resistance in order to inform policymakers about the product's efficacy [53].

3.2. *Aedes aegypti* mosquito resistance to pyrethroids

Pyrethroids are artificial versions of pyrethrins, naturally occurring insecticidal esters of chrysanthemum acid classified as I and II based on their physical characteristics and toxicity [12]. To keep the action potential of the insect system constant, synthetic pyrethroid insecticides act by blocking ion channel axons. VGSC protein is the binding site for synthetic pyrethroids to regulate nerve impulses. As a result of received nerve impulses and resulting in continuous stimulation (seizures), insects will experience hyperexcitation (anxiety) and seizures [38]. It is this toxic effect of permethrin that kills these larvae. The 0.2% and 0.4% cypermethrin used showed resistance. The toxic effects of cypermethrin as a contact and

stomach poison induces larval death by entering the central nervous system and convulsions, and paralysis within minutes [31].

0.05% cypermethrin resistance was documented in several regencies/cities in the Central Java Province, including Semarang, Klaten, Kudus, and Gombong [14], [19], [23], [54], in addition to Pekanbaru [18]. Cypermethrin is reportedly tolerable in other parts of Indonesia, including Riau Islands, Malang, Makassar, and other towns and districts [21], [22], [24]. In Surabaya and Balikpapan, different situations have developed that make people more susceptible to lambda-cyhalothrin [32], [33]. Operational variables resulting from long-term use of cypermethrin continuously cause the occurrence ofresistance, tolerance, and sensitivity to pyrethroids [14], [18], [19], [23], [54]; dosages used above those supported by such long-term usage will result in resistance [55]. Operational parameters that affect the *Aedes aegypti* mosquito's sensitivity include technique, dosage, application time, and frequency [17].

Insects' central nervous systems can be reached by pyrethroids, which can pierce the chitin layer and lymph, causing paralysis due to the sensations they receive. Biological variables can also lead to circumstances of resistance. To quickly spread across the *Aedes aegypti* mosquito population, resistant mosquitoes will undergo genetic alterations and develop resistance gene [15]. These early indications of insecticide resistance will be crucial in helping to launch effective control measures that will prevent the development of mosquito resistance, such as rotating insecticides or adding a catalyst to increase the effectiveness of insecticides in Indonesian mosquito control programs [56]. Resistance incident strongly advise ongoing monitoring of insecticide resistance and prudent insecticide selection and use to manage the resistance phenomena [57]–[59].

3.3. Resistance of *Aedes aegypti* larvae to temephos

Temefos is an organophosphate insecticide that is effective for killing mosquito larvae; this is because temefos works by inhibiting enzymes in the insect nervous system [56], temephos that can damage the neurotransmitter system [60]. Temephos will block cholinesterase, causing neurological diseases. This situation happens when acetylcholine accumulates into choline and acetic acid, inhibiting the enzyme and preventing the breakdown of the acetylcholine that would otherwise result in the larvae's death [61]. The esterase enzyme, which is more significant in *Aedes aegypti*, aids in the detoxification process. If the esterase enzyme's activity increases, a resistance mechanism occurs [62], [63]. Genetic, biological-ecological, and operational variables, circumstances for quick or slow resistance to emerge depending on how long and how frequently the pesticide is used, the number of mosquito breeding sites supplied with the treatment, and the incorrect dose are all potential causes of resistance [64], [65]. Some areas that experience resistance in Pesisir Selatan Regency, West Sumatra Province; this is due to the use of insecticides to eradicate mosquito nests coupled with the continuous use of pesticides as pesticides in agriculture [46], and it is present in endemic regions that have also seen temephos resistance in Kulon Progo Regency, Special Province of Yogyakarta (D.I Yogyakarta) [45] in Tegal Regency, Central Java Province [66]. The WHO-established criteria for resistance in these locations, which call for 80% mortality at a concentration of 0.02 ppm for both endemic and sporadic areas, are met [45].

Due to the use of temephos being appropriate given the amount of material and water in the water reservoirs and maximizing community empowerment through eliminating mosquito nests and 3M, several other regions in Indonesia reported whether endemic or non-endemic areas were still susceptible to the temephos [48]. This is because temephos is rarely used in Okus, Bombana, and Sleman Regencies since it is thought that it will alter the quality of the water and is dangerous for everyday usage [47], [50], [67]. The active ingredient's capacity to kill larvae, exposure time, the test circumstances for the larvae, temperature, and humidity all impact the sensitivity status of *Aedes aegypti* larvae to temephos [68]. Utilizing insecticides with diverse chemical structures and applying them in a rotation approach is crucial to limit the emergence of resistance [69]. Temephos can be used to combat the rise in dengue fever cases during the rainy season. Still, it is also important to be aware of the possibility of cross-resistance, which does not entirely rule out the possibility that *Aedes aegypti* larvae will become resistant to temephos alone but can also be accompanied by resistance to malathion or pyrethroids, making control more challenging [70]. Since dengue fever is endemic in most of Indonesia, efforts must be made to combat the disease through enhancing community empowerment and enlisting the political support of the local government for programs to destroy mosquito breeding grounds [69].

4. CONCLUSION

In DHF endemic areas, *Aedes aegypti* mosquitoes have developed resistance to pesticides from the pyrethroid and organophosphate families, according to a study of papers collected in Indonesia, including organophosphate groups such as malathion, pyrethroid groups such as cypermethrin and deltamethrin. The condition of resistance to *Aedes aegypti* is not only in endemic areas but also in metropolitan areas. If

pesticides are to be applied in susceptible and tolerant areas using an insecticide-type rotation plan and recommended levels, they should be monitored and evaluated. In addition, there must be an expansion of the community empowerment movement toward eradicating mosquito nests.

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APPENDIX

Table 1. Characteristics of studies on pesticide resistance in *Aedes aegypti* sp mosquitoes that were included in the research (*contiune*)

Author	Title	Journal	Research design	Sample	Research result
[14]	Mosquito Resistance as a Potential Vector of Dengue Hemorrhagic Fever (DHF) in Semarang City, Indonesia	Jurnal Ilmu Kehidupan Tropis	Cross sectional	15-20 households in each hamlet in Semarang to use ovitraps to gather mosquito eggs	*Aedes aegypti* mosquitoes' resistance to pyrethroids was 77.8% of 278 mosquitoes tested biochemically, based on observations of monooxygenase enzymes. *Aedes aegypti* and Aedes albopictus are resistant to pyrethroids
[15]	*Aedes aegypti* mosquito resistance test against 0.05% cypermethrin at Sungai Duku harbor and Syarif Kasim II Airport Pekanbaru	SEHATI jurnal Kesehatan Vol. 1 No. 1:16-21	Cross sectional	250 mosquitoes	The findings demonstrated that *Aedes aegypti* at the Sultan Syarif Kasim II Airport and Sungai Duku Harbor region tolerated 0.05% cypermethrin. The *Aedes aegypti* mosquito population at Sultan Syarif Kasim II Airport and Sungai Duku Harbor was equally susceptible to 0.05% cypermethrin.
[16]	Susceptibility Status of *Aedes aegypti* Mosquitoes to Cypermethrin Insecticides in the Perimeter and Buffer Areas of Tanjung Emas Port, Semarang City	Jurnal Vektora	descriptive observational	240 Ae mosquitoes, seven officers, and three officers/cadres at the Bandarharjo Health Center are undertaking the vector control/fogging program.	Showed that *Aedes aegypti* in the buffer and perimeter regions were still vulnerable using the WHO standard bioassay test, with 100% death of the test mosquitoes collected from the two research sites. According to biochemical testing, *Aedes aegypti* remained vulnerable to 0.05% cypermethrin, with 100% death in both research regions. According to the findings of program managers' interviews, all of the officers used the active ingredients of insecticides, malathion and cypermethrin appropriately to perform standards, operations, and fogging activities. Both kinds of pesticides have been applied alternately. The pesticide rotation, however, has yet to be done regularly.
[17]	Lambdacyhalothrin Resistance Test Against *Aedes aegypti* Mosquitoes in Seaport Areas	Jurnal Kesehatan Lingkungan	observational	20 *Aedes aegypti* mosquitoes in mature form	The death rate of test and control mosquitoes after being exposed to 0.05% lambda-cyhalothrin for 30 minutes served as the basis for the test results. It was noted how many of the 20 examined mosquitoes fell in the following time intervals: 1, 5, 10, 20, 30, and 1 hour. The RT 14 Prapatan Village, Balikpapan *Aedes aegypti* mosquito is resistant to 0.05% lambda-cyhalothrin.
[18]	Resistance of *Aedes aegypti* to Insecticides: A Study on Household Insecticides	JIK Vol. 15 No. 2 Hal. 63-68	Cross sectional	450 mosquitoes	Insecticide X contains the active chemicals cypermethrin, transfluthrin, and importin; insecticide Y, transfluthrin; and insecticide Z, which has pyrethrin and cyfluthrin, are three types of insecticides that are commonly used on the market. Applying the pesticide on filter paper, the adult mosquitoes were subjected to each insecticide for an hour before being inspected the following day. According to WHO standards, mosquitoes with a death rate of less than 80% are resistant. Long-term continuous usage may be the cause of this tendency for resistance.

Table 1. Characteristics of studies on pesticide resistance in *Aedes aegypti* sp mosquitoes that were included in the research (*contiune*)

Author	Title	Journal	Research design	Sample	Research result
[19]	Resistance of Ae. Aegypti against Cypermethrin in Klaten District, Central Java	Jurnal Kesehatan Lingkungan Ruwa Jurai Vol. 15 No. 1: 1-7	Observational	Ngawonggo Village, Kajen, Meger	All samples, ranging from moderate to resistant levels, showed cypermethrin resistance, according to the study's findings. Cypermethrin resistance was detected in samples from one subdistrict (89% mortality after 30 minutes). Moderate resistance was present in two more subdistricts, with 97% mortality after 30 minutes.
[20]	Exploration of the Degree of Resistance of *Aedes aegypti* Mosquitoes to Cypermethrin 0.05% Insecticides in Dengue Hemorrhagic Fever Cases in Kudus District in 2017	Keslingmas Vol. 37 No. 3: 240-404	Descriptive	Fifty homes with larvae were chosen from each of the sub-two district sub-districts.	Malang Regency's *Aedes aegypti* is resistant to 0.05% Cypermethrin, with mortality rates of 90% in Turen, Kepanjen, 96% in Karangploso, and 100% in Dau, with an average of 94%. This demonstrates that a concentration of 0.05% of Cypermethrin is still effective in lowering the growth of *Aedes aegypti*. However, the application rotation must still be considered to decrease the incidence of dengue.
[21]	Analysis of Resistance Status of Ae aegypti to 0.05% Cypermethrin Insecticide in Endemic Districts, Malang Regency	Jurnal Ilmiah Biologi Vol. 10 No. 1: 240-251	Observational Descriptive	4 Districts, Turen, Kepanjen, Dau, and Karangploso	Malang Regency's *Aedes aegypti* is resistant to 0.05% Cypermethrin, with mortality rates of 90% in Turen, Kepanjen, 96% in Karangploso, and 100% in Dau, with an average of 94%. This demonstrates that a concentration of 0.05% of cypermethrin is still effective in lowering the growth of *Aedes aegypti*, but the rotation of application must still be taken into account to lower the incidence of dengue.
[22]	Susceptibility Test for Malathion and Cypermethrine (Cyf 50 EC) Insecticides on Ae aegypti Mosquito Populations in Makassar City and Barru District	Higiene Vol. 4 No. 1: 41-47	Quasi experimental	900 female adult *Aedes aegypti* mosquitoes, 35 days old	Results for cypermethrin (Cyf 50 EC) 1.5% were 17.95 minutes, 29.42 minutes, 32.67 minutes, and 38.77 minutes; results for 328.87 minutes (5 hours), 1639.06 minutes (27 hours), 2196.94 minutes (37 hours), and 3243.43 minutes (54 hours). Malathion insecticide produced 25.18 minutes, 55.37 minutes, 63.93 minutes, and 79.99 minutes in the Barru District, whereas cypermethrin (Cyf 50 EC) 1.5% produced yields of 21.77 minutes, 41.76 minutes, 47.42 minutes, and 58.05 minutes.
[23]	Efficacy of Cypermethrin Type Insecticide Against *Aedes aegypti* Mosquitoes in the Fogging Program at PKU Muhammadiyah Gombong Hospital	Buletin Kesehatan Lingkungan Masyarakat, Vol. 40 No. 3:126-135	Exploration with a quantitative approach	10 *Aedes aegypti* mosquitoes	With three replications, the test mosquitoes' average mortality resulted in a yield percentage of 67%. When mosquito mortality falls below 80%, the mosquito is considered inefficient or resistant to the pesticide Cypermethrin 15 ml.
[24]	Susceptibility Status of *Aedes aegypti* Mosquitoes to Sipermethrin Insecticide at Tanjung Balai Karimun Harbor, Riau Archipelago Province	Jurnal Kesehatan Masyarakat Vol. 8 No.6: 752-756	descriptive	240 mature mosquitoes of the first generation.	*Aedes aegypti* mosquitoes from Tanjung Balai Karimun's port demonstrated that they remained vulnerable to cypermethrin pesticides in the buffer and perimeter areas, respectively, by 98.75% and 100%.

Table 1. Characteristics of studies on pesticide resistance in *Aedes aegypti* sp mosquitoes that were included in the research (*contiune*)

Author	Title	Journal	Research design	Sample	Research result
[25]	The Effect of Lambdacyhalothrin on the Resistance Status of *Aedes aegypti* in the Buffer Area of Juanda International Airport, Surabaya	Journal of Public Health Science Research Vol. 3 No. 1: 1-9	experimental analytics	150 mosquitoes	Based on calculations made from the test findings, 98.67% of the examined mosquitoes died after being corrected, completing the degree of susceptibility of *Aedes aegypti* in the Juanda International Airport's buffer zone in Surabaya susceptible by WHO standards.
[26]	Rural Dengue Strain Vector Resistance to Malathion 5%	Jurnal Kesehatan Masyarakat Indonesia, Vol. 15 No. 1: 6-9	Cross sectional	20 houses	The kind of *Aedes aegypti* is determined by the findings of watching the larvae in the Batursari Village Area RW 30, RW 3, and RW XX. Mosquito fainting happened on average every 2.8 minutes after exposure to 5% malathion. For all locations with 5% Malathion, mortality is at 100%.
[27]	*Aedes aegypti* vector resistance status on malation and activity of non-specific esterase enzymes in Tembalang district, Semarang city	Jurnal Kedokteran dan Kesehatan Indoensia Vol. 10 No. 3:215-221	Cross sectional	480 houses	According to the bioassay, the death rate of *Aedes aegypti* in 12 villages in the Tembalang District ranged from 0 to 62% after 24 hours of testing with impregnated paper. In Rowosari, Kedungmundu, Sambiroto, and Meteseh, the mechanism of resistance that increased non-specific esterase enzyme activity in -naphthyl acetate was not observed; however, it started to appear in low percentages (15%) in Sendang Mulyo, Tandang, Sendangguwo, and Bubusan, and average rates (45-75%) in Tembalang, Jangli, and Mangunharjo. *Aedes aegypti* in Kramas exhibits the mechanism of high esterase enzyme activity with AV0.700-0.900 with a percentage of 20% and AV0.900 with a rate of 80%.
[28]	Resistance Status of *Aedes aegypti* Mosquitoes to Malathion and Ace-1 Gene Mutations in Ambon City	Jurnal Vektor Penyakit Vol. 14 No. 2:119-128	Cross sectional	100 mosquitoes	*Aedes aegypti* mosquitoes from the Waihaong and Rijali Health Centers had no alterations in the ace-1 gene. Two health facilities in Ambon City have been classed as having tolerant *Aedes aegypti* mosquito resistance, while 14 additional health centres have been categorised as having susceptible resistance. At the Waihaong and Rijali Public Health Centers in Ambon City, there is no evidence of the ace-1 gene in *Aedes aegypti* mosquitoes.
[29]	Entomology Survey, Susceptibility of *Aedes aegypti* to Organophosphate Insecticides, and VGSC Gene Identification in Dusun Malangrejo, Sleman Yogyakarta	Aspirator Vol. 11 No. 1: 37-44	Cross sectional	house located within a radius of 100 meters from the DHF sufferer's house in Malangrejo Hamlet	The *Aedes aegypti* mosquito may nest in bathtubs. Malathion resistance was 13.75%, whereas *Aedes aegypti* remained tolerable to temefos (95.4%). Biological and biochemical experiments demonstrate the possibility of pesticide resistance, which is linked to enhanced non-specific esterase enzyme activity. Both the genes (V1016G; S989P) and F1534C produced promising findings for the VGSC gene identification.
[30]	Resistance Status of the *Aedes sp* Mosquito Against Malathion in Papkelan Village, Minahasa Regency	JKL Vol. 9 No. 1 :56-61	Observational Descriptive approach	25 mosquitoes	*Aedes sp.* mosquitoes die at a rate of 8% to 16% within the first hour of the measurement. At the same time, a 24-hour measure shows a yield of 64%–76% of the death of *Aedes sp.* mosquitoes, with an average of 9% mortality. Malathion usage for an extended period results in resistance to

Table 1. Characteristics of studies on pesticide resistance in *Aedes aegypti* sp mosquitoes that were included in the research (*contiune*)

Author	Title	Journal	Research design	Sample	Research result
					Aedes sp. with an average death rate of 70%. The use of the pesticide malathion (0.8%) in the Papakelan Village has resulted in the resistance status of *Aedes sp.*
[31]	Correlation of Entomological Index to *Aedes aegypti* Susceptibility in Six Types of Insecticides in Seven Provinces of Sumatra Region	Jurnal Ekologi Kesehatan Vol. 18 No. 2:70-79	Cross sectional	100 houses	The highest HI and CI values were found in Pematang Siantar City (58.60% and 64%). In comparison, the lowest values were located in Prabumulih Regency and Palembang City (22.70% and 0%), the highest BI was found in West Bangka Regency (87.40%), the lowest in Metro City (31.10%). The highest ABJ was located in Palembang City (77.30%) and the weakest in Pematang Siantar City (4 In 7 Provinces in the Sumatra Region, the 0.8% Malathion pesticide is still effective as a method of mosquito control with a strong and moderate association to the Container Index (CI) and House Index (HI).
[32]	Mapping Resistance of Ae sp Mosquitoes to Malathion and Dengue Hemorrhagic Fever (DHF) Density in North Sulawesi	Jurnal Sehat Mandiri Vol. 15 No. 1: 1-7	Descriptive	100 houses	In four city districts with resistant DHF mosquito vectors and one district (Minahasa Utara), there is an average density of HI (31%), BI (17.5%), and CI (34.8%) vectors with resistance status. Digital maps of the resistance and density vectors are created.
[33]	Entomological Survey and Susceptibility Status of *Aedes aegypti* Larvae to Organophosphate Insecticides in Banguntapan Village, Yogyakarta	BALABA, VOL. 15 No. 1: 41-48	Cross sectional	400 houses	One hundred and forty-nine (149) of the 696 containers examined tested positive for *Aedes aegypti*, including ABJ (73%), HI (27%), BI (33%), CI (18.14%), and PI (17.5%). The most popular breeding places for larvae are bird troughs, buckets, plant pots, and bathtubs. *Aedes aegypti* is vulnerable to temefos, although organophosphate pesticides are relatively resistant to it biochemically. A bathtub is the most likely place for *Aedes aegypti* to spawn in Banguntapan Village, which falls under the category of probable sites for dengue virus transmission from a vector to people.
[34]	Dengue Hemorrhagic Fever Mosquito Dengue (*Aedes aegypti*) Dengue Density and Resistance Status Against Malathion in Bitung City in 2017	Proceedings of the 2018 Manado Health Polytechnic National Seminar, Volume 1 Number 3	Observational Descriptive	100 houses	The results of the vector density study, namely the House Index (HI) value of 44, Container Index (CI) value of 21.4, and Breteau Index value of 73, all indicate high larval density, and the results of the WHO standard susceptibility test and 0.8% malathion impregnation paper test for *Aedes aegypti* mosquito susceptibility status test, which measured the mosquitoes' sensitivity to the chemical by counting how many died an hour and a, Therefore, start a new rotation of insecticides right away after testing the one that will be applied.
[35]	Resistance Status of Dengue Hemorrhagic Fever (*Aedes aegypti*) Vector to 1% Fenitrothion Insecticide in Kudus District, Central Java Province in 2017	Keslingmas Vol. 37 No. 4: 405-534	Descriptive	4 Districts, 50 houses per kelurahan/village	The findings of the susceptibility test technique, which involved impregnating paper with 1% Fenitrothion, indicated that test mosquitoes from the districts of Kaliwungu, Kota Kudus, and Jati died at a rate of 100%. In comparison, the district of Mejobo exhibited a mortality percentage of test

Table 1. Characteristics of studies on pesticide resistance in *Aedes aegypti* sp mosquitoes that were included in the research (*contiune*)

Author	Title	Journal	Research design	Sample	Research result
					mosquitoes of 98.67%.
[36]	Susceptibility Test of *Aedes aegypti* Mosquitoes Against Malathion Insecticides in Fogging Areas, Malang Regency	Jurnal Ilmiah Biologi Vol. 9 No. 2: 378-388	Observational Descriptive	3 Districts, Kepanjen, Gondanglegi and Bantur	In the districts of Kepanjen, Gondanglegi, and Bantur, the test mosquito fatality rates were 98%, 93%, and 96%. This demonstrates that, to the extent of 0.8%, the *Aedes aegypti* mosquitoes in three different locales were considered resistant to the pesticide malathion.
[37]	Exploration of the Resistance Status of *Aedes Sp* Mosquitoes to Biochemical Organophosphate Insecticides in Banyumas Regency in 2017	Jurnal Kesehatan Lingkungan Vol. 38 No. 1: 1-123	Explorative Research	Kedungrandu Village and Sidamulih Village	The independent T-Test statistic test, which had a significance value of 0.565, revealed no difference between the two villages in terms of the esterase enzyme content in mosquito bodies, indicating that *Aedes Sp* mosquitoes in both villages had essentially the same exposure to organophosphate insecticides. According to the study, 8.33% of *Aedes sp.* mosquitoes in Kedungrandu Village were determined to be resistant to organophosphate class pesticides, whereas Sidamulih Village had 1.36% more tolerable insects than Kedungrandu Village.
[38]	Susceptibility Status of *Aedes aegypti* to Organophosphate and Pyrethroid Insecticides in Indonesia	Jurnal Ekologi Kesehatan	Cross sectional	3 districts/cities, 3 puskesmas and each puskesmas determined 1 village, RW/hamlet with high DHF cases	The findings indicated that 50 (49%) districts were resistant to temephos, 30 (29%) districts were tolerant, and 22 (22%) districts were sensitive. The sensitivity of Ae aegypti to temephos was 0.02%. One district (1%), according to the findings of the 0.05% cypermethrin pesticide test, was tolerant, whereas 100 (98%) districts were resistant. According to test results on alpha-cypermethrin 0.025%, 4 (9%) districts were sensitive, 18 (40%) districts were tolerant, and 23 (51%) districts were resistant. Deltamethrin 0.025% test findings showed 14 (14%) susceptible districts, 22 (22%) tolerant districts, and 66 (65%) resistant districts.
[39]	Molecular Detection of Gene Resistant To Various Insecticides In *Aedes aegypti* AT Banyuwangi East Java Using Polymerase Chain Reaction	Jurnal Kedokteran Hewan	Cross sectional	25 *Aedes aegypti* mosquito larvae	The Banyuwangi Regency's *Aedes aegypti* mosquito is resistant to 0.8% malathion and 0.25% cypermethrin. In Banyuwangi Regency, a gene encoding VGSC with a 250 bp band was discovered using the polymerase chain reaction (PCR) method. This gene is linked to resistance to pyrethroid (cypermethrin) and organophosphate (malathion) pesticides in *Aedes aegypti* mosquitoes.
[40]	Resistance Status of the *Aedes aegypti* Mosquito from the Working Area of the Salido Health Center to Malathion 5% and Alpha-cypermethrin 0.025%	Jurnal Ilmu Kesehatan Indonesia	Descriptive	3-5-day-old adult *Aedes aegypti* mosquitoes that have 240 sugars	After 24 hours with 5% malathion, 95% of *Aedes aegypti* mosquitoes died, with LT50 at 624 minutes and LT90 at 1,247 minutes. After 24 hours, 0.025% alpha-cypermethrin killed 96.25% of *Aedes aegypti* mosquitoes, with LT50 being 526 minutes and LT90 being 1,163 minutes.
[6]	Resistance of *Aedes aegypti* to Organophosphate and Synthetic	BALABA Vol. 14 NO. 1 95-106	Cross sectional	Female *Aedes aegypti*, 3–5 days old	All of the research areas in Deli Serdang showed that *Aedes aegypti* remained resistant to alpha-cypermethrin and deltamethrin.

Table 1. Characteristics of studies on pesticide resistance in *Aedes aegypti* sp mosquitoes that were included in the research (*contiune*)

Author	Title	Journal	Research design	Sample	Research result
	Pyrethroid Group Insecticides in North Sumatra and Jambi Provinces				Malathion and cypermethrin are two insecticides that are often used in both provinces. According to the study's findings, dengue fever control programs in North Sumatra and Jambi provinces can employ alpha-cypermethrin as a substitute pesticide since it is still efficient at combating *Aedes aegypti*.
[41]	Entomology Indicators and Resistance Status of *Aedes aegypti* Larvae and Mosquitoes to Household Insecticides in Three Regencies/Cities in West Sumatra Province	Jurnal Vektor Penyakit Vol 13 No. 2 97-106	Cross sectional	100 houses in the working area of 3 health centers, 300 houses in 1 province and 900 3 districts/cities	The monitoring entomology indicators are still in the moderate range. The mosquito breeding environment consists of disposal containers that are positive for larvae at a rate of 9.94% and control containers that are positive for larvae at a rate of 90.27%. Deltamethrin and alphacypermethrin, two commonly used insecticides, still exhibited sensitivity and tolerance, respectively, but malathion, Lambdacyhalothrin, and cypermethrin were resistant. The south coast and Bukit Tinggi were resistant to the larvicide temephos, which controls larvae.
[42]	Status of the Susceptibility of *Aedes aegypti* Mosquitoes to Malathion 5% and Alpha-cypermethrin 0.025% in the Work Area of the Belimbing Health Center, Kuranji District, Padang City	Jurnal Kesehatan Andalas Vol. 9 No. 1 22-28	Experimental	140 *Aedes aegypti* mosquitoes	After 24 hours, 98% of *Aedes aegypti* mosquitoes were killed with 5% malathion, with LT50 and LT90 being 76 and 853 minutes, respectively. After 24 hours, 0.025% alpha-cypermethrin killed 87% of *Aedes aegypti* mosquitoes, with LT50 and LT90 being 264 and 1500 minutes, respectively.
[43]	Resistance Status of *Aedes aegypti* to 0.8% Malathion and 0.05% Cypermethrin at Pulau Baai Port, Bengkulu City	Jurnal Kesehatan masyarakat Vol. 8 No. 2: 243-249	Quasi Experimental	408 female mosquitoes	The average death rate of *Aedes aegypti* mosquitoes in the perimeter region and the buffer port of Baai Island did not differ, according to the study of *Aedes aegypti* mosquito mortality data using an independent t-test. *Aedes aegypti* mosquitoes living on the island of Baai Harbor were resistant to 0.8% malathion and 0.05% cypermethrin (death 90%), according to the results of the susceptibility investigation. According to the findings of the interviews with respondents, 79% of families used pyrethroid pesticides, and 83.87% of respondents used insecticides overall. Type 53.78%, fuel 20.17%, lotions 21.85%, pesticide sprays, and mosquito netting were utilized by responders.
[44]	Exploration of *Aedes sp* Mosquito Resistance with Susceptibility Method Using Malathion 0.8% and Lamdacylotrin 0.03% Insecticides	Kesehatan Lingkungan Masyarakat Vol. 38 No. 4: 305-364	exploration	every house where there are larvae and eggs of *Aedes sp* mosquitoes with a distance of 100 meters from the case index house in each cardinal direction	Malathion insecticide 0.8% revealed a mortality rate of 8.75% in Kedungrandu Village, Patikraja District, and 15% and 11.25% in Sidamulih Village. At the same time, Lamdacyhalotrin 0.03% in Sidamulih Village is 92.5% and 100% in Kedungrandu Village, respectively.

Table 2. Characteristics of the findings of articles included in the study of insecticide resistance in *Aedes sp*

Author	Title	Journal	Research design	Sample	Research result
[45]	Resistance Status of Dengue Virus Serotype in *Aedes aegypti* on the Exposure of Insecticide Temefos and Cypermethrin	Jurnal Aisyah: Jurnal Ilmu Kesehatan Vol. 5 No. 2 215-220	observasional analitik kasus kontrol	There were 25 *Aedes* F1 female larvae and aegypti adult larvae.	Wonosidi Lor and Dipan, both Gadingan endemic locations, are still entirely vulnerable to temefos. Sporadic places like Driyan, which has a Mortality Rate (AK) of 100%, are in a vulnerable position, whereas Durungan and Kriyanan are in a tolerant status (AK=88% and 97%). Potentially susceptible locations include Kauman and Janten (AK=100% and 98%), whereas Panjatan is classified as tolerable (AK=84%). All endemic, sporadic, and prospective regions are 80% or more resistant to the pesticide cypermethrin.
[46]	Entomology Survey, Mayan Index, and Susceptibility Status of *Aedes aegypti* Mosquito Larvae to Temephos	Jurnal Kesehatan Andalas Vol. 7 No. 1 33-41	Cross sectional	100 houses	Obtained a high-density value (HI) of 57%, 22.04% CI, and 123% BI with an average value of DF 7. With a total of 558 containers, the CS value of 77.42% was more significant than the DS value of 22.58%. Ninety-three buildings with low risk and seven houses with medium risk were found using the Maya index. Resistance was discovered during a Temephos 0.012 susceptibility test.
[47]	The Resistance Status of *Aedes aegypti* Larvae to Temephos in Depok, Sleman, Yogyakarta	Indonesian Journal of Pharmacology and Therapy Vol. 2 No. 1:17-21	Quasi experimental	Instar 3 *Aedes aegypti* larvae obtained from RW 9 and 10 Minomartani Village	This 0.02 ppm was administered to the treatment group for 24 hours. The study is reported as a percentage of larval mortality and resistance categories based on WHO recommendations. In RW 9, 100% of *Aedes aegypti* larvae were present, compared to 97% in RW 10. Temephos is still effective against *Aedes aegypti* larvae in Depok District, Sleman, at a level of 0.02 ppm.
[48]	Resistance status of *Aedes aegypti* larvae to the use of Themefos in DHF endemic areas in Maros Regency in 2020	Jurnal Sulolipu: Media Komunikasi Sivitas Akademika dan Masyarakat Vol. 21 No. 1 :6-13	Experimental	endemic area of Maros Regency	The results of the tests, which were conducted six times, revealed that the status of larvae/larvae for 1GR bats (temefos) is still susceptible according to the Permenkes Regulation No. 50 of 2017 and 1975 WHO standards. The reasons and fundamental factors to ascertain the condition of the *Aedes aegypti* vector for the use of temefos are based on the situation as a DHF endemic area and the control efforts that have been made using larvicides within a specific time frame. The results obtained can be used to determine techniques and subsequent control measures.
[49]	Density and Vulnerability Status of *Aedes aegypti* Larvae in Pancur Pungah Village, Muara Dua District, Okus Regency in 2019	Jurnal Kedokteran dan Kesehatan Vol. 7 No. 2: 99-105	Observational descriptive	100 houses	The larvicidal test revealed that all larvae exposed to Temephos 0.02 ppm perished, with results of HI: 35, CI: 14.1 and BI: 55. These calculations show that the vector density is at a moderate intensity and that Temephos sensitivity is still there.
[50]	Susceptibility Status of *Aedes sp* Larvae to Organophosphate Insecticides in East Poleang District	Indonesian Journal for Health Sciences Vol. 4, No. 2: 108-114	Quasi Experimental with Post Test Only With Control Group Design	625 larva *Aedes aegypti* 625 *Aedes aegypti* larvae	The percentage of larval death after 24 hours was 100% in all five hamlets. This study demonstrates that *Aedes spp*. Larvae are still sensitive to the temefos insecticide dosage of 0.02 ppm. Based on WHO larval susceptibility status criteria, *Aedes spp.* are still vulnerable if the death rate of the larvae is 98–100%. The one-sample T-test findings yielded a value of p=0.00.
[42]	The Vulnerability of the *Aedes aegypti* Mosquito in the Tegal Dengue Endemic Area, Central Java	BALABA	Experimental	100 houses	Larvae of *Aedes aegypti* died at a rate of 0.025 ppm at 90%. At LC50 of 0.0005 ppm and LC99 of 1.1037 ppm, permethrin kills *Aedes aegypti* at a 26% rate at each concentration. Lt50 was at 661,636 minutes, and LT99 was at 5958807,272 minutes. Susceptibility Although *Aedes aegypti* is resistant; its larvae may not be.