Review Article

Insecticide Resistance in the West Nile Encephalitis, Japanese Encephalitis, Avian Malaria and Lymphatic Elephantiasis Vector, Culex pipiens complex (Diptera: Culicidae) in Iran

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Abstract

Background: *Culex pipiens* complex is considered as a vector of some important diseases such as West Nile fever, equine encephalitis, Rift valley fever, St. Louis encephalitis, Elephanthiasis and avian malaria in the world. The main measure for vector control is using insecticides. High use of insecticides caused resistance in the populations. The aim of this study was to review the status of insecticide resistance in the vector.
Methods: Insecticide resistance in this species was found by the available papers and map of the data for carbamates, organochlorine, organophosphates, pyrethroids, microbial and insect growth regulator insecticides were done. An intensive search of scientific literature was done in “PubMed”, “Web of Knowledge”, “Scopus”, “Google Scholar”, “SID”, and related resources.
Results: Results showed that a wide variety of resistance to different insecticides in the country. Due to importance of this species in transmission of diseases.
Discussion: resistance management strategies should be further considered to prevent from in secticide resistance and replacement of novel approach for vector control.

Keywords: Insecticide; Resistance; Vector; Culex pipiens complex

Introduction

Mosquitoes are the most important vectors of pathogens in the world (1). The *Culex pipiens* complex from the Culicinae subfamily includes the subspecies *Cx. pipiens pipiens*, *Cx. p. pipiens* form molestus, *Cx. p. quinquefasciatus*, *Cx. p. ausralicus*, *Cx. p. globocoxitus* and *Cx. p. pallens* (2). In recent studies, the species *Cx. pipiens* and *Cx. quinquefasciatus* have been identified as two separate species by molecular methods (3,4). The global distribution of this species is shown in Fig.1. *Cx. pipiens* in Iran has two biological forms of *Cx. pipiens pipiens* and *Cx. pipiens molestus*. Two subspecies are almost semi-domesticated and are found in most subtropical regions (4). The biological form of *Cx. pipiens* form pipiens is mainly found in rural areas, is very interested in the blood of the host bird, preferably lays eggs in stagnant water and outside human habitation, has winter diapause and is non-autogenous. The biological form of *Cx. pipiens* form

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molestus has autogenic behavior and lacks winter diapause (3). In addition to causing allergies and disturbances, the *Cx. pipiens* complex transmit the highest number of pathogens compared to other vectors (4). *Cx. pipiens* transmit several diseases such as West Nile fever (WNF), equine encephalitis (EE) , Rift valley fever (RFV), St. Louis encephalitis (SLEV) , some worm pathogens such as *Dirofilaria immitis* and *Wuchereria bancrofti*, as well as some avian malaria protozoa such as *Plasmodium relictum* and *Plasmodium gallinaceum* (5) (Fig.2). In recent years, *Cx. pipiens* has been accused of transmitting the Zika virus in some African countries and the United States (6,7). The preference for taking blood from birds, which are mainly hosts of disease agents and sometimes arbovirus, has led to a widespread global distribution of zoonotic diseases. The distribution and distribution of *Cx. pipiens* is also very effective on the process of economic development resulting from the tourism industry. The increase in abundance and morphological and physiological characteristics in *Cx. pipiens* has caused that after malaria vectors, more attention should be paid to the control of this species (7,8).

The best and most standard method of the WHO to control vector-borne diseases is to use vector control methods (9-12). Vector control is performed by one of the biological, physical, and chemical methods. The fast effect in a short time and easy access to chemical compounds have made most of the methods of control of mosquitoes depend on these compounds. Chemical control may be carried out at the larval stage as a larvicide or in the adult stage by various methods such as residual spraying, spatial spraying, and insecticide-impregnated mosquito nets. One of the oldest methods of chemical control of *Culex* mosquitoes in Iran is the use of oily compounds on the surface of the water, which causes their death by covering the breathing siphon in the larva stage. After that, the use of mineral compounds became common for controlling measures. Among the chemical compounds, four groups of organochlorine, organophosphates, carbamates, and pyrethroids are in the first place. Organochlorine insecticides were first introduced to the world in 1939 by Paul Muller. Organochlorine insecticides with disruption of the vital enzyme Ca-Mg ATPase and imbalance in the axonal transmission system cause repeated and sequential irritation, convulsive movements, paralysis, and eventually insect death. Organophosphate insecticides are esters of phosphoric acid. The toxic properties of these compounds were first discovered in 1937 by Schrader. Organophosphate insecticides are the most diverse and widely used toxins

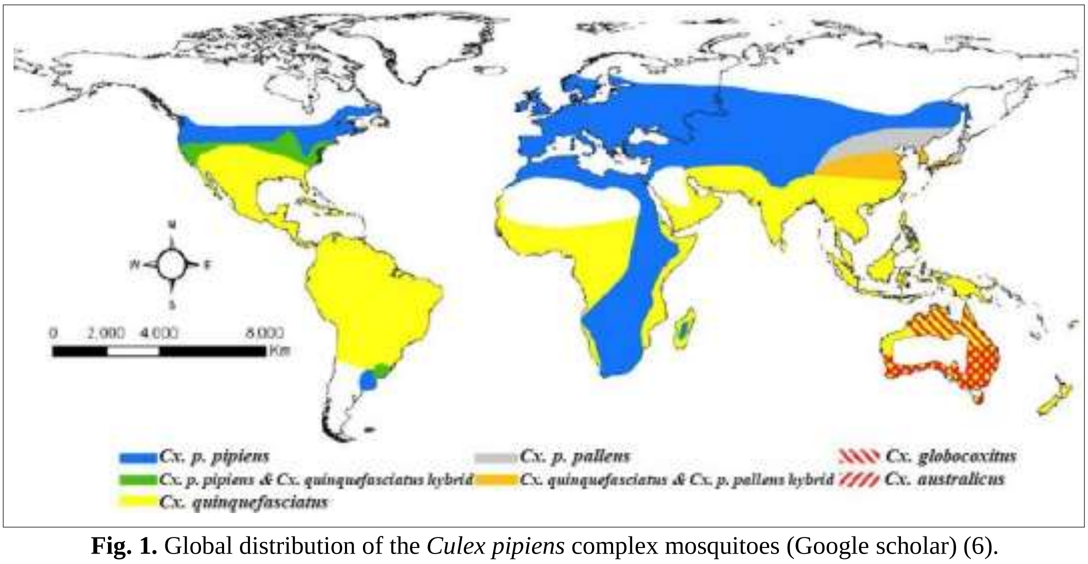

Fig. 1. Global distribution of the *Culex pipiens* complex mosquitoes (Google scholar) (6).

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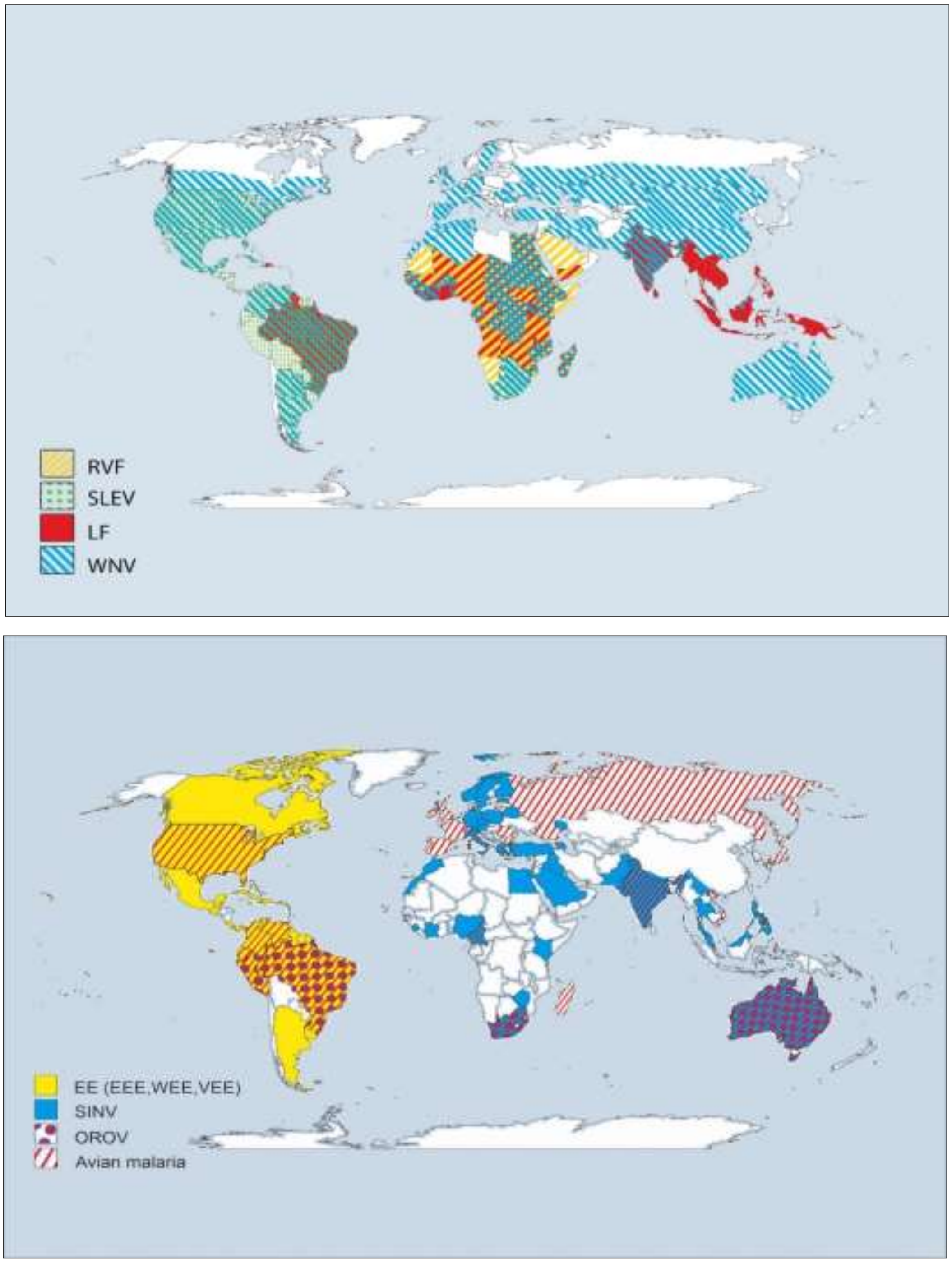

Fig. 2. Global distribution of diseases transmitted by *Cx.pipiens* complex(Google scholar)

in agriculture and public health. The rapid effect, absence of hazardous residues, and lack of cumulative property of common point are important. Organophosphate insecticides disrupt the nerve function of insects and kill them by inactivating the enzyme acetylcholinesterase and accumulating acetylcholine at the synapse site.

Pyrethroid insecticides are of plant origin and their insecticidal properties were first discovered in Iran in 1763 from the flowers of the pyrethrum plant. Insecticidal properties of pyrethroids are derived from the keto alcoholic esters of chrysanthemum and pyrethroid acids. The core of this group of insecticides is cyclopropane carboxylate. Rapid decomposition, lack of hazardous residues, and lack of cumulative properties are characteristic of pyrethroid compounds Pyrethroid insecticides affect the sodium channels and lead to the paralysis of the insect. In many parts of the world, Pyrethroid insecticides are used in the form of insecticide-impregnated mosquito nets and indoor spraying to control adult mosquitoes. Carbamate insecticides were first identified in 1940 by Grysin. The main insecticide carbamate is physostigmine, which is extracted from the extract of *Physostigma venenosum*. Carbamate insecticides are organic compounds of carbamic acid derivatives (H_2NCOOH) whose functional group is carbamate esters. Carbamate insecticides kill insects by reversibly inactivating the acetylcholinesterase enzyme. The most widely used carbamate insecticide used in health programs is carbaryl.

The use of chemical pesticides was very effective and useful at first, but gradually and with increasing consumption, it caused environmental hazards, harmful effects on human health, and, most importantly, resistance in *Culex* mosquitoes and other vectors. This phenomenon creates staggering costs in the countries involved. Major countries fighting the *Culex* mosquito are also infected with malaria, and various species of Anopheles mosquitoes are found in these countries. Close ecological and biological characteristics such as larval habitat have made *Culex* mosquitoes resistant to most of the insecticides used against malaria vectors. The phenomenon of resistance is the most important problem in the fight against mosquitoes and other vectors and makes it more difficult every day to fight the pathogens transmitted by vectors. According to the World Health Organization, the phenomenon of insecticide resistance is an inherited or acquired trait that allows an insect to tolerate different doses of one insecticide or a combination of several insecticides. According to the standard of the WHO, when the insect mortality rate is less than 90%, the so-called resistant species, if the mortality rate is between 90% and 97%, the species is tolerant, and if the mortality rate is 98% and more be, the species is sensitive (13- 26).

Materials and Methods

Data Collection

In this study, the data were collected from Internet sources, contacts with organizations and institutes and reports of the World Health Organization (WHO). In online sources, we searched published articles on *Cx. pipiens* resistance and Iran in PubMed, Scopus, ISI, Literature Retrieval System (AFPMB), IranMedex, Google Scholar, and related resources. Using the keywords

Table 1. The resistance of *Culex pipiens* against organochlorine insecticides in different regions of Iran

Reference	year	Province	Pesticides	LT_{50} (min)	KT_{50} (min)	Resistance status
Salim-Abadi et al.	2015	Tehran City	DDT 4%	-	-	Resistant
Ghorbani et al.	2018	Mazandaran (Sari County)	DDT 4%	-	-	Resistant
			Dieldrin 4%	-	-	Resistant
			Dieldrin 0.4%	-	-	Resistant
Salim-Abadi et al.	2017	Kerman (Rafsanjan County)	DDT 4%	139	-	Resistant
Rahimi et al.	2019	Tehran (southern)	DDT 4%	240	1567	
Vatandoost et al.	2004	Tehran(Varamin County)	DDT 4%	-	-	Resistant
Naseri et al.	2015	West Azerbaijan	DDT 4%	-	-	Resistant
Fathian et al.	2014	Siatan & Baluchistan (Chabahar)	DDT 4%	31.93	-	Resistant
Zeidabadi et al.	2017	Tehran(Qarchak)	DDT 4%	78.39	-	Resistant
Ataie et al.	2015	East Azarbaijan	DDT 4%	134.75	-	Resistant

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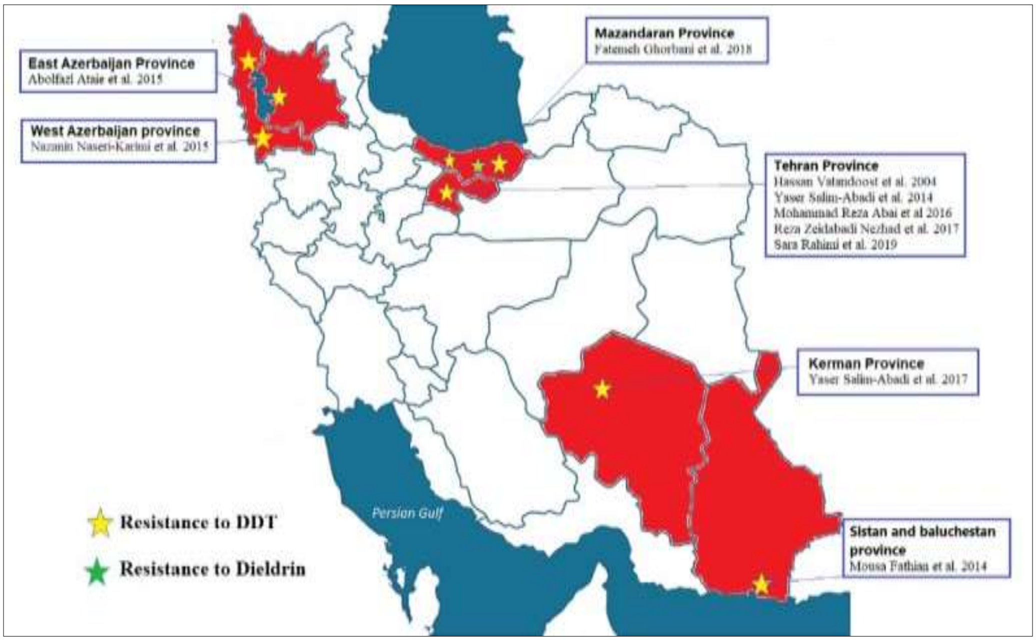

Fig. 3. The resistance of *Culex pipiens* against organochlorine insecticides in different regions of Iran

Table 2. The resistance of *Culex pipiens* against organophosphate insecticides in different regions of Iran

Reference	year	Province	Pesticides	LT_{50} (min)	KT_{50} (min)	Resistance status
Ghorbani et al.	2018	Mazandaran (Sari)	Malathion 5%	-	-	Resistant
			Fenitrothion 1%,	-	-	Resistant
			Malathion (1ppm)	-	-	Resistant
			Temephos (0.02)	-	-	Resistant
Salim-Abadi et al.	2017	Kerman (Rafsanjan)	Malathion 5%	33	-	Resistant
Rahimi et al.	2019	Tehran (southern)	Malathion 5%	29.7	74.5	
Vatandoost et al.	2004	Tehran (Varamin)	Malathion 5%	-	-	Tolerant
Fathian et al.	2014	Siatan &Baluchistan	Malathion 5%	-	-	Susceptible
Abai et al.	2016	Tehran	Temephos	LC50: 0.18	-	Resistant
Ataie et al.	2015	East Azarbaijan	Malathion 5%	8.02	-	Tolerant

resistance, organophosphate, pyrethroid, organochlorine, carbamate, IGR, and P450, kdr, monooxygenase, glutathione, or esterase. Main data were collected and classified then analyzed using the software.

Results and discussion

In Iran, various insecticides have been used against *Cx. pipiens*. According to standard studies, the *Cx. pipiens* has are resistant to some of Organochlorine insecticides such as DDT 4% in the cities of Varamin, Tehran, Qarchak, Islamshahr, Chabahar, Tabriz, Urmia, Sari, and Rafsanjan and against the insecticide Dieldrin 4% in the city of Sari has shown resistance (Table 1) (Figure 2).

Among organophosphate insecticides *Cx. pipiens* was susceptible to Malathion 5% in Chabahar Sari and Rafsanjan and tolerated in Azerbaijan and Varamin. *Cx. pipiens* is also resistant to Fenitrothion 1% in Sari and Temephos in Tehran and Sari (Table 2, Fig. 3).

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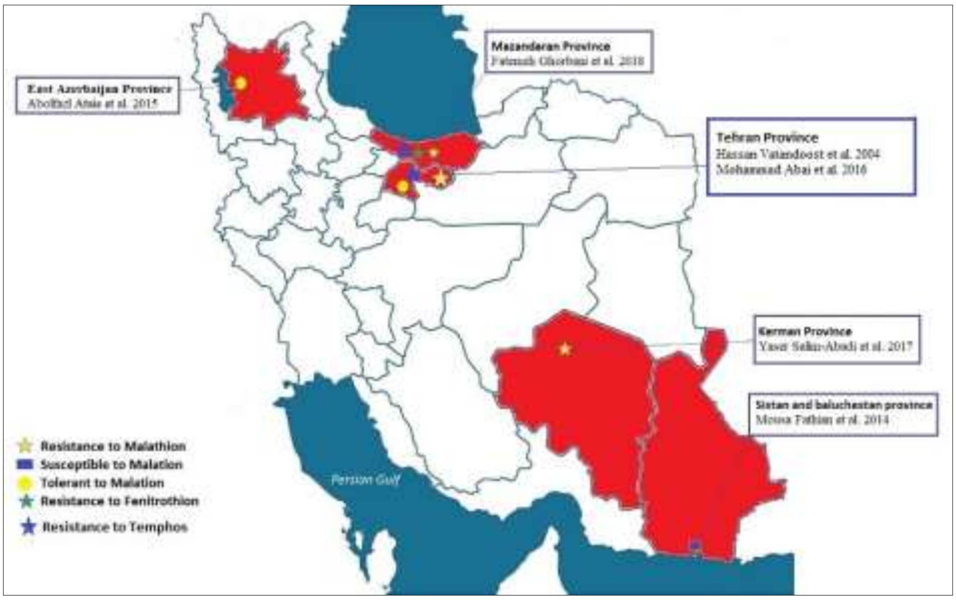

Fig. 4. The resistance of *Culex pipiens* against organophosphate insecticides in different regions of Iran

Table3. The resistance of *Culex pipiens* against carbamate insecticides in different regions of Iran

Reference	year	Province	Pesticides	LT50 (min)	KT50 (min)	Resistance status
Ghorbani et al.	2018	Mazandaran (Sari)	Bendiocarb 0.1%	-	-	Resistant
			Propoxur 0.1%	-	-	Resistant
Salim-Abadi et al.	2017	Kerman (Rafsanjan)	Bendiocarb 0.1%	27	-	Resistant
Rahimi et al.	2019	Tehran (southern)	Bendiocarb 0.1%	73	139	
			Propoxur 0.1%	60.3	140.1	
Vatandoost et al.	2004	Tehran (Varamin)	Bendiocarb 0.1%	-	-	Resistant
Fathian et al.	2014	Siatan & Baluchistan	Propoxur 0.1%	-	-	Resistant
Ataie et al.	2015	East Azarbaijan	Propoxur 0.1%	36.10	-	Resistant

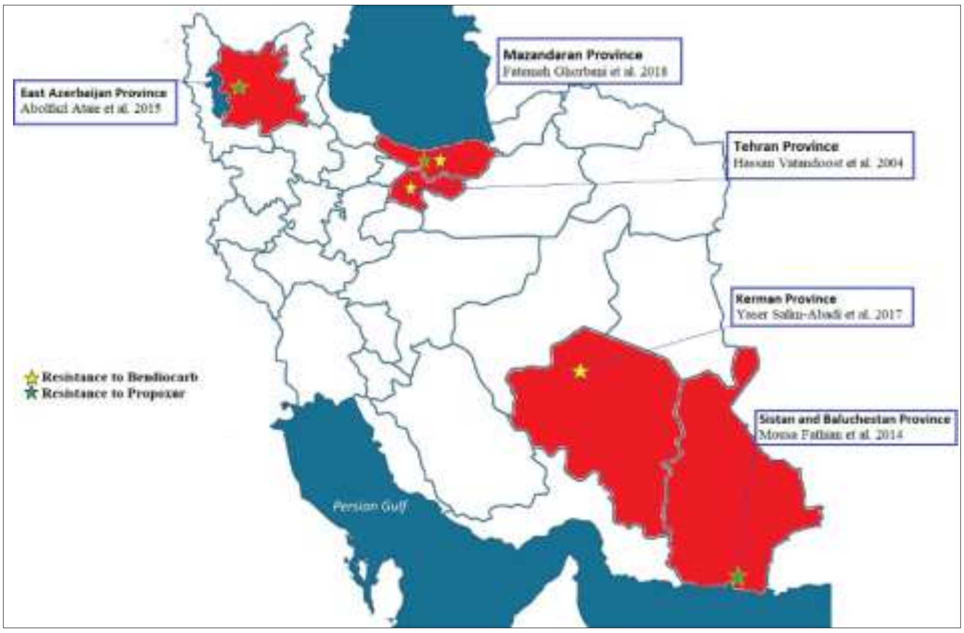

Fig. 5. The resistance of *Culex pipiens* against carbamate insecticides in different regions of Iran

Table 4. The resistance of *Culex pipiens* against pyrethroid insecticides in different regions of Iran

Reference	year	Province	Pesticides	LT_{50} (min)	KT_{50} (min)	Resistance status
Salim-Abadi et al.	2015	Tehran City	DDT 4%	-	-	Resistant
Ghorbani et al.	2018	Mazandaran (Sari County)	DDT 4%	-	-	Resistant
			Dieldrin 4%	-	-	Resistant
			Dieldrin 0.4%	-	-	Resistant
Salim-Abadi et al.	2017	Kerman (Rafsanjan County)	DDT 4%	139	-	Resistant
Rahimi et al.	2019	Tehran (southern)	DDT 4%	240	1567	
Vatandoost et al.	2004	Tehran(Varamin County)	DDT 4%	-	-	Resistant
Naseri et al.	2015	West Azerbaijan	DDT 4%	-	-	Resistant
Fathian et al.	2014	Siatan & Baluchistan (Chabahar)	DDT 4%	31.93	-	Resistant
Zeidabadi et al.	2017	Tehran(Qarchak)	DDT 4%	78.39	-	Resistant
Ataie et al.	2015	East Azarbaijan	DDT 4%	134.75	-	Resistant

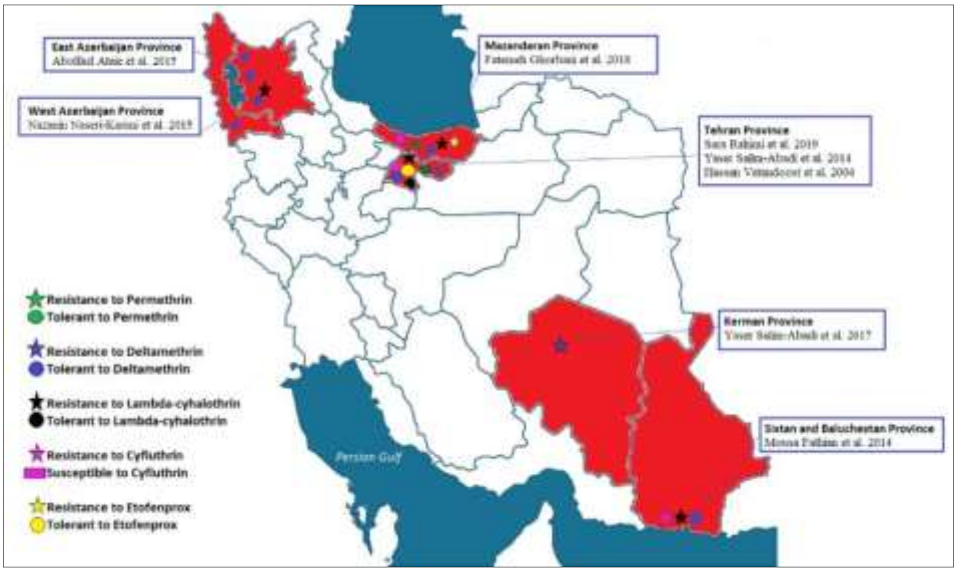

Fig. 6. The resistance of *Culex pipiens* against pyrethroid insecticides in different regions of Iran

Among carbamate insecticides, this species has shown resistance to Bendiocarb 0.1% in Rafsanjan, Sari and Varamin counties and resistance to Propoxur 0.1% in Chabahar, Sari, and Tabriz counties (Table 3, Fig. 4).

The highest diversity of insecticide used against *Cx. pipiens* in Iran is related to a pyrethroid insecticide. *Cx. pipiens* tolerates permethrin 0.75% in Varamin city. It is resistance in Sari city Tehran, West Azerbaijan. It is tolerant to deltamethrin 0.05% in Chabahar, Tabriz and Varamin counties. *Cx. pipiens* is tolerant to Lambdacyhalothrin 0.05% in Varamin city and has shown resistance in Tehran, Chabahar, Tabriz, Rafsanjan, Uromia and Sari cities. *Cx. pipiens* is susceptible to Cyfluthrin 0.15% in Varamin city and resistant to Chabahar, Sari and Tehran cities. *Cx. pipiens* also tolerant against Etofenprox 0.5% in Varamin city and resistant in Sari city (Table 4, Fig. 5). There are also several reports of insecticide resistance in the world (26-36).

Analysis of data from various researches in Iran shows that *Cx. pipiens* complex is resistant to DDT 4%. Mechanism of similar effect between DDT and pyrethroid insecticide. Examination of the maps revealed that the areas where the *Cx. pipiens* species that have shown resistance to the insecticide DDT is similar to the areas where the species has shown resistance to the pyrethroid insecticide. Therefore, in these areas, the use of these two groups of insecticides in control programs should be avoided. Analysis of article data also showed that in Tehran and Mazandaran provinces, *Cx. pipiens* species have shown resistance against most of the tested insecticides, so in these two provinces, insecticides with different mechanisms of action should be used.

Conclusion

According to the WHO guideline there are several insecticide are being used for control of mosquitoes as Indoor residual spraying, fogging, larviciding and insecticide treated net (37). Monitoring and mapping of insecticide resistance is a vital guideline for authorities to provide appropriate measure for vector control.

Conflict of Interest

The authors declare that there is no conflict of interest.

Acknowledgments

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