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RESEARCH ARTICLE

MONITORING AND MAPPING OF INSECTICIDE RESISTANCE IN MALARIA VECTOR, *ANOPHELES SACHAROVI* IN IRAN (1997-2020)

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ABSTRACT

Malaria is the main vector borne diseases worldwide. According to the recent record of World Health Organization, 228 million cases have been reported in 2018 mainly in in African region**.** One of the main important measures for vector control is using insecticides. Monitoring and mapping of insecticide resistance is the main measure for appropriate decision. All the date published about resistant status of *Anopheles sacharovi* were searched on Pubmed, Elsevier, Springer, Web of Science, Iranmedex, Majiran, google scholar, etc. The results showed that there is widespread, resistance/tolerance to different groups of insecticides in the country. Monitoring and mapping as well as detection of mechanisms of insecticide resistance is appropriate for vector control decision. The results of resistant of this malaria vector to different WHO insecticides will provide an appropriate guideline for the Ministry of health and Medical Education of the country for appropriate vector control.

KEYWORDS

Anopheles sacharovi, insecticide resistance, malaria, vector, Iran.

1. INTRODUCTION

Malaria is the main vector borne diseases worldwide. According to the recent record of World Health Organization, 228 million cases have been reported in 2018 mainly in in African region (WHO, 2019). According to the report of Ministry of Health of Iran, less than 89 locally-transmitted cases in 2017 have been reported. The aim of country is to eliminate the disease by 2025 (Vatandoost et al., 2019). Iran is now launching the elimination of malaria. Different studies have been conducted during more than 90 years on malaria and its vectors in Iran. The last checklist of Iranian mosquitoes shows 31 *Anopheles* species including sibling, biological forms and genotypes, 17 out of them are reported to be included in malaria transmission. These vectors are considered as sibling, genotype and type forms. *Anopheles stephensi, An. culicifacies, An. fluviatilis, An. dthali* are the main vector species of south-eastern foci, while *An. sacharovi* and *An. maculipennis* are included in malaria transmission in northwest focus, and *An. superpictus* has wide distribution in all malaria foci of the country. Seasonal activity of *Anopheline* mosquitoes varies in different area due to environmental condition. It shows one peak in northwest especially in summer, however, there are two peaks of activity in coastal warm and humid region in the southern part of Iran with oriental epidemiological characteristics.

Campaign against malaria vectors was started from 1952 by DDT spraying and then replaced by dieldrin, malathion, propoxur, lambdacyhalothrin and deltamethrin, respectively. The chemical control of vectors now is restricted to endemic malarious areas of south-eastern part of the country with Deltamethrin and residual spraying and long-lasting permethrin impregnated nets (Olyset) for personal protection, while biological control is conducting by *Bacillus thuringiensis* as larvicide. In this article we will present the status of insecticide resistance to different imagicides including DDT 4%, diledrin 0.4%, malathion 5%, fenitrothion 1%, bendiocarb 0.1%, propoxur 01. %, lambdacyhalothrin 0.1% and 0.05%, deltamethrin 0.025% and 0.05%, permethrin 0.25% and 0.75%, cyfluthrin 0.15%, and etofenprox 0.5% based on review of published data from 1957 to 2012. Knowledge on insecticide resistance in target species is a basic requirement to guide insecticide use in malaria control programmes in local and global scales. The main criteria for susceptibility status, which are recommended by WHO, were considered. The results showed that there is widespread, multiple resistance in the country in *An. stephensi,* and DDT resistance in some other vectors (Vatandoost et al., 2009; Abbasi et al., 2019).

Malaria is still a major endemic disease in foci located in south and southeast of Iran. It is unstable with two seasonal peaks mainly in spring and autumn. These areas include the provinces of Sistan and Bluchistan,

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Hormozgan and Kerman (Manouchehri et al., 1992). In this part of the country six anopheline mosquitoes including *Anopheles culicifacies*, *An. stephensi*, *An. dthali*, *An. fluviatilis*, *An. superpictus*, and *An. pulcherrimus* are known to be the malaria vectors, while *An. sahacrovi* and *An. maculipennis* are considered as malaria vector in northern part of the country (Manouchehri et al., 1972, 1976, 1992; Zaim 1987; Zaim et al., 1993, 1995; Yaghoobi-Ershadi et al., 2001; Zahirnia et al., 2001; Vatandoost et al., 2004, 2006; Sedaghat et al., 2005; Vatandoost et al., 2007; Hanafi-Bojd et al., 2011, 2012). Limited malaria risk exists from March to November in rural areas of the provinces of Sistan-Baluchistan, Hormozgan and Kerman (tropical part); in some areas north of the Zagros Mountains and in western and southwestern regions during the summer months. *Plasmodium vivax* is dominant agent of malaria in Iran, while *P. falciparum* is reported and infects about 5% of patients, although cases due to the second parasite have dropped in recent year (Ministry of Health and Medical Education).

So far 31 species from 2 subspecies (*Anopheles* and *Cellia*), siblings, genotype and type forms are recorded in the country, 17 out of them are in complexes or groups that introduced as malaria vectors. *Anopheles sacharovi* is one of the members of maculipennis complex and confirmed as malaria vector in some parts of its distribution area (Faghih 1969; Saebi 1987; Yaghoobi-Ershadi et al., 2001; Azari-Hamidian et al., 2004; Sedaghat and Harbach 2005; Azari-Hamidian, 2007; Hanafi-Bojd et al., 2011). *Anopheles sacharovi* is reported from coastal parts of Italy, Sardinia, Corsica, Croatia, Republic of Macedonia, Albania, Bulgaria, Romania, southern regions of the former USSR, Turkey, Lebanon, Israel, Jordan, Syria, Iraq and Iran. It is the most important malaria vector in Turkey, northwest border of Iran Twenty years ago, an epidemic of malaria occurred in northwestern Iran, where *An. sacharovi* was identified as the vector. This species is distributed from northwest to southeast of Iran Alongside the Zagros Mountains (Figure 1).

A human blood index of 38.5% shows the high tendency of this Anopheles species to human hosts This species has a good potential for malaria transmission to humans, where the infected host is available. It is also regarded as the principal potential vector in regions of southern Europe. *Anopheles sacharovi* was responsible for malaria transmission in Greece in 2011. (Hanafi-Bojd et al., 2018). Agriculture in Iran remains highly sensitive to climate developments; the country's most important crops are wheat, rice and other grains, sugar beet, fruits, nuts, cotton, and tobacco, which require the use of insecticides. So far different groups of insecticides are using for crops protection in the country. The main governmental use of insecticide in the health sector is their application for adult mosquito control.

The campaign against malaria vectors started with organochlorines (DDT, dieldrin and BHC) during the 1960's, followed by organophosphates (malathion and pirimiphos-methyl) for 2 decades from 1966 and continued with the carbamate, propoxur during 1977-1990, and then with pyrethroids including lambdacyhalothrin and Deltamethrin (Manouchehri et al., 1992; Edrissian et al., 2006). Temephos, reldan and pirimiphos-methyl was used for larviciding from 1970 to 1992. Malaria control in the country is now based on use of deltamethrin (5% WP) as an adulticide and *Bacillus thuringiensis* as a larvicide at volumes of about 15 and 5 tons respectively (Manouchehri et al., 1992; Edrissian et al., 2006; CDC annual reports). The main important aim of current study is to provide an appropriate guideline for the local, neighboring and international countries to control of this important malaria vector

2. Materials and Methods

2.1 Data collection and analysis

Published data about insecticide susceptibility of Anophline mosquitoes in Iran were searched from different sources including: PubMed, Elsevier, Springer, Web of Science, Iranmedex, Majiran, Google scholar, etc. Within the collected documents, criteria for the bioassay tests and results were followed as defined by WHO (1981, 1998). According to the WHO guideline the following criteria is classified. Morality between 98-100% indicating susceptible, mortality between 90-97% indicating tolerant and mortality under 90% indicating the resistant. An excel sheet was created for insecticide resistance based on the applied insecticide at diagnostic dosage recommended by WHO. ArcGIS 9.3 used for mapping geographical distribution of malaria vectors and spatial pattern of insecticide/larvicide resistance.

3. Results and Discussion

Anopheles sacharovi is a major vector of malaria in the central plateau of Iran and is widely distributed in central, northwest, west, southwestern and Fars province in the south of the country (Hanafi-Bojd et al., 2011). In 1957 for the first time *An. sacharovi* were tested against DDT 4% in Fars province. Results showed that this species was susceptible to DDT 4%. In 1957 DDT was used for malaria vector control in the region. In 1957-73 the mortality of *An. sacharovi* to DDT 4% decreased to 35-40% indicating occurrence of resistance in this population (Zulueta, 1959, Manouchehri et al., 1974). Due to DDT resistance, dieldrin was replaced for vector control since 1961. Subsequently after 2 years of dieldrin, application resistance to this insecticide was reported (Manouchehri and Zaini 1973). In 1967 malathion was used in the region and until 1973 there was no report of malathion resistance in this population (Vatandoost et al., 2006; Vatandoost et al., 2009; Vatandoost et al., 2013). A study in by showed that *An. sacharovi* collected from Kazerun region, is susceptible to DDT, but they found resistant to fenitrothion 1% (Figure 2) (Ghavami and Ladonni, 1998). Results of the susceptibility tests in 1998 (Figure 3) indicated this species is resistant to DDT and dieldrin, and tolerant to propoxur, deltamethrin and permethrin in Parsabad and Germi counties in Ardebil province, northwest of Iran (Yahoobi-Ershadi et al., 2001). In this area reported resistance of this *Anopheles* to DDT, and its tolerance to dieldrin, bendiocarb, lambdacyhalothrin, permethrin and etofenprox (Figure 4) (Salari Lak et al., 2002). They found this species susceptible to other insecticides including propoxur, malathion, fenitrothion, deltamethrin and cyfluthrin. Current study on susceptibility status of *An. sacharovi* in East-Arzerbaijan, northwest of the country confirmed its resistance to DDT and tolerance to dieldrin (Figures 5,6) (Vatandoost and Abai, 2012). Table 1 presents the susceptibility status of this Anopheles based on reviewed documents, while figures 6-7 mapped the distribution of this species in the country as well as its resistance to insecticides (Vatandoost et al., 2004, 2005; Vatandoost and Abai 2012; Vatandoost and Zahirnia 2010; Vatandoost and Hanafi-Bojd, 2012). There are reports of insecticide resistance of *An. sacharovi* to some insecticides in neighboring countries, i.e. Turkey and Iraq (Manouchehri et al., 1980; Kasap et al., 2000).

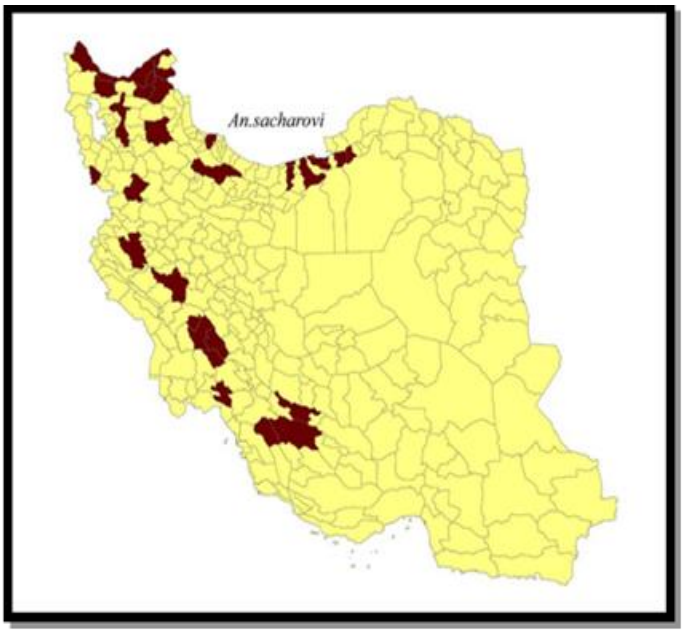

Figure 1: Distribution map of *Anopheles sacharovi* in Iran

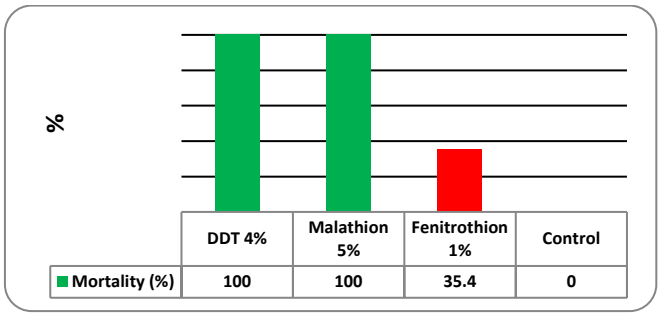

Figure 2: Susceptibility status of *An. sacharovi* to different insecticides in Dashte Arzhan area, Fars Province, Southern Iran, 1997

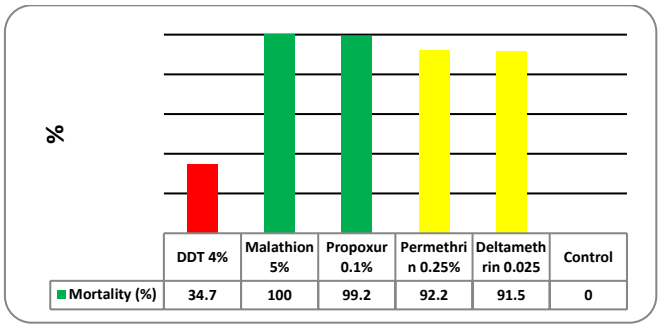

Figure 3: Susceptibility status of *An. sacharovi* to different insecticides in Parsabad County, Ardabil Province, Northwest of Iran, 1998

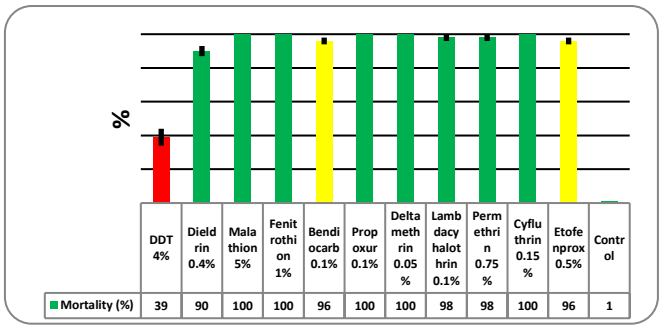

Figure 4: Susceptibility status of *An. sacharovi* to different insecticides in Poldasht County, West Azarbijan Province, Northwest of Iran, 2001

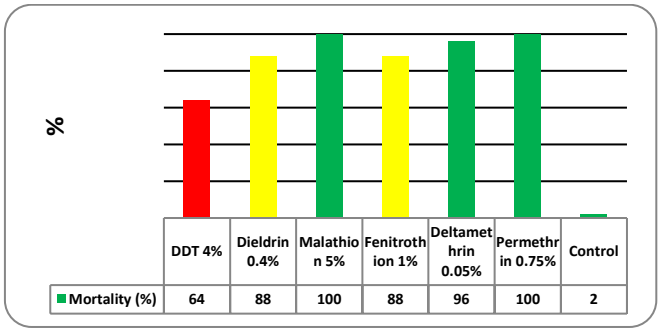

Figure 5: Susceptibility status of *An. sacharovi* to different insecticides in East Azarbijan Province, Northwest of Iran, 2010

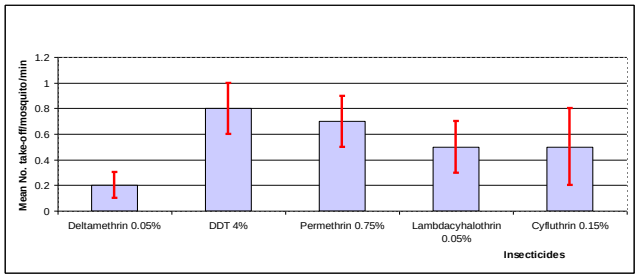

Figure 6: Comparative performance of irritability of *An. sacharovi* to different insecticides, East Azarbijan, Northwest of Iran, 2010

Table 1: Status of insecticide resistance in *Anopheles sacharovi* of Iran, 1957-2012

Insecticide	*An. sacharovi*
DDT 4%	R
Dieldrin 0.4-4%	T
Malathion 5%	S
Fenitrothion 1%	R
Propoxur 0.1%	S
Bendiocarb 0.1%	T
Permethrin 0.25-0.75%	T
Lambdacyhalothrin 0.025-0.1%	S
Deltamethrin 0.025-0.05%	T
Cyfluthrin 0.15%	S
Etofenprox 0.5%	T

S = Susceptible, T= Tolerant, R = Resistant

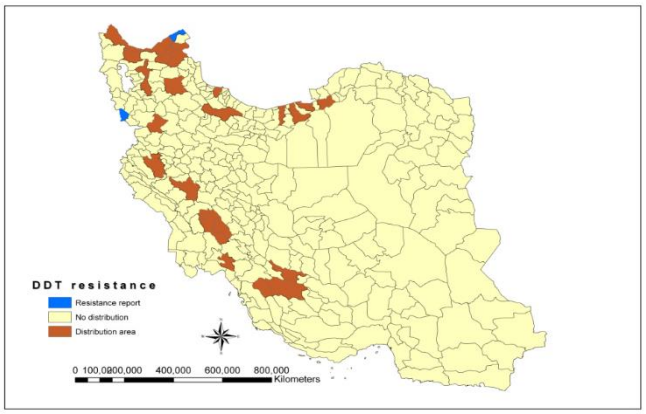

Figure 7: Distribution map of *An. sacharovi* and spatial distribution of resistance to DDT in Iran, 1997-2010

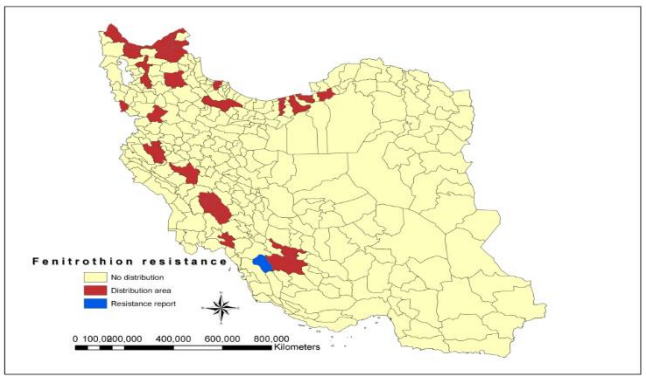

Figure 8: Distribution map of *An. sacharovi* and spatial distribution of resistance to Fenitrothion in Iran, 1997-2010

4. Conclusion

Extensive resistance/tolerance to insecticides from different classes is found in An. sacharovi. It is an alarm for malaria vector control authorities to manage the insecticide application in the intervention programmes. There are several works in the country on different aspects of malaria including insecticide resistance monitoring, using bed nets and long-lasting impregnated nets, vector control. Monitoring of insecticide resistant in the country is essential for appropriate vector control strategies. Malaria vector control in the country is responsible of ministry of Health and Medical Education. There are several measures for malaria vector control as Indoor residual spraying, using insecticide impregnate bed net and larvicidng. The results of current study will provide a guideline ro appropriate control of malaria vector.

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