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Insecticide susceptibility status of malaria vectors in India: A review

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ABSTRACT

Malaria is a disease caused by the biting of the Anopheline mosquito vectors. Vector control is the major component of the strategy for malaria control which aims to prevent parasite transmission through interventions targeting adult malaria vectors. For this, chemical, biological and mechanical methods are applied. In chemical approach of controlling malarial mosquitoes, insecticides have been used extensively for larviciding, indoor residual spraying and impregnation of bed nets in the last few decades. As a result of this, vector resistance to these insecticides have been recorded in various parts of the country and mosquitoes have developed wide spread resistance to some of these insecticides. There is need for countrywide and regular surveys for monitoring the insecticide susceptibility status of major vectors and assessing their implications on vector control activities. In India, most of the studies revealed that resistance against DDT is prevalent in most of the malaria vector species. Bye and large, *An. culicifacies* and *An. stephensi* are resistant to malathion also and resistance against synthetic pyrethroid is developing. Moreover, *An. fluviatilis*, *An. minimus* and *An. annularis* are susceptible to malathion and deltamethrin. As the chemical molecules available for the role of insecticide are very few and invention of new molecules takes time, this is the need of time that increasing trend of resistance status of mosquitoes against the insecticides used in the vector control programme have to be minimized. There are only a few reports on the susceptibility status of the mosquitoes against various insecticides and thus more emphasis on these studies should be given. Again the appropriate use of the insecticides like rationale use with rotation of insecticides and insecticide combinations can be an effective strategy to combat this insecticide resistance.

Keywords: Malaria vector; Insecticide susceptibility; review; India

1. Introduction

Malaria is a main cause of mortality and morbidity among human population of India. This disease is caused by the biting of the mosquito vectors. In India, *Anopheles culicifacies*, *An. stephensi*, *An. fluviatilis*, *An. minimus*, *An. dirus* and *An. sundaicus* are six primary and *An.* varuna, *An. annularis*, *An. philippinensis* and *An. jeyporiensis* are four secondary vectors of malaria [1]. In addition to these, *An. subpictus* has also been reported as a potential malaria vector [2]. Vector control is a major component of the global strategy for malaria control which aims to prevent parasite transmission mainly through interventions targeting adult Anopheline vectors [3]. Before the Ross discovery, stagnant water was suspected to be responsible for malaria and thus management of water was the key method for vector control. Kerosene was used successfully as a larvicide during 19th century. During the first quarter of the 20th century, mosquito control was mainly done by interfering its breeding. For this, chemical, biological and mechanical means were applied. In chemical approach of controlling mosquito breeding, vegetable oil, kerosene oil, Paris green, DDT emulsion in kerosene, Chlordan, Aldrin and Dieldrin have been used as larvicides. Paris green was successfully used as a larvicide to control mosquito population particularly in Assam. Larvivorous fishes like *Gambusia* and Guppy, and exposure to sunlight and shading also were used as a biological means to check mosquitoes breeding. On a small scale, some mechanical mode of control like surface drains, vertical drains and subsoil drains were also used. After the World War II, insecticide with residual properties; mainly DDT, was used to control mosquito populations. This mode of vector control gained much success in vector control programmes. On account of continued use of synthetic insecticides particularly DDT and BHC under malaria control programme, selection of resistant populations has occurred amongst many mosquito vector species. In India, evidence of resistance was first reported by Pal *et al*. (1952) in *Culex fatigans* [4].

Ongoing strategies of vector control rely heavily on the use of safe and effective insecticides through indoor residual spraying (IRS) or insecticide-treated nets (ITNs). Pyrethroids are the only option for the treatment of mosquito nets due to their relative safety for humans at low dosage, excito-repellent properties, rapid rate of knock-down and killing effects [5]. The regular use of these insecticides in IRS activities and impregnation of bed nets in the vector control programme had a very good impact as a transmission control measure in the beginning, but later vector resistance to these insecticides was recorded in certain parts of the country and mosquitoes have developed resistance to a varying degree depending on the use of insecticide. Anopheline mosquitoes exhibit two major mechanisms of insecticide resistance: metabolic resistance and target site insensitivity. Metabolic resistance to insecticides is usually associated with enhanced levels or modified activities of detoxification enzymes; esterases, Glutathione S-Transferase (GST), or Mixed Function Oxidases (MFO), while target site insensitivity results due to modifications in GABA receptors, or point mutations in the voltage-gated sodium channel gene, often termed as kdr (knock-down resistance) [6-8].

Comprehensive knowledge of the factors underlying resistance is needed for the implementation of efficient vector control programmes including resistance management strategies. This raises the need for countrywide and regular surveys for monitoring the insecticide susceptibility status of major vectors, detecting resistance genes and assessing their implications on vector control activities [9]. In India, the status of insecticide susceptibility of the mosquito vectors has been reviewed earlier form time to time (Pillai 1996, Roop Kumari *et al*. 1998, Mittal *et al*. 2004) [7, 10-11]. The present paper is an attempt to review the present insecticide susceptibility status of malaria causing mosquitoes in India based on the reports published during the last one decade.

We searched for studies in which insecticides were tested against malaria vectors in India and insecticide resistance was reported. Public data base were also searched with relevant key words. Abstracts were read and full research papers were retrieved pertaining to insecticide resistance and causes of resistance in dengue vectors under review with reference to India.

2. *Anopheles culicifacies*

An. culicifacies is the most prevalent malaria vector species found throughout the rural plain areas in India. It is primarily a zoophagic species, which is a complex of five sibling species namely sp. A, sp. B, sp. C, sp. D [12] and sp. E. All the sibling spp. (except sp. B) are efficient vectors in different areas of the country, while sp. B is a poor vector species [13]. Initially indoor residual spraying with DDT was used for the control of this species. But gradually *An. culicifacies* has developed resistance against DDT and it was the first mosquito species to develop resistance against this insecticide [14]. Now *An. culicifacies* is resistant to DDT in almost all parts of the country [11]. Recent reports have either confirmed or added some more areas, where *An. culicifacies* were not reported as resistant to DDT [15-26] (Table 1). In the year 1969, malathion was introduced in vector control programme in mosquito control in DDT resistant areas [27]. However soon after its introduction, Rajagopal reported double resistant *An. culicifacies* in Gujarat and Maharashtra states of India in 1977 [28]. Mittal *et al*. (2004) reported varying degree of resistance to malathion in *An. culicifacies* in different parts of the country [11]. In recent years various other workers have studied susceptibility status of malaria vectors against malathion. Shukla *et al*. reported partial resistance (80-100 mortality) in *An. culicifacies* from Moradabad (U.P.) and Uttarakhand state [20, 29]. Similarly mortality ranging from 4-100% was observed in Jharkhand, Chhattisgarh, Rajasthan, Maharashtra and Madhya Pradesh [15-18, 30-33]. These reports indicate that, *An. culicifacies* has developed varying degree of resistance to malathion in the country. In 1990’s synthetic pyrethroids like deltamethrin were introduced in national vector borne disease control programme (NVBDCP) erstwhile national malaria eradication programme. But very soon resistance was reported against deltamethrin also. Mittal *et al*. (2002), for the first time, reported reduced susceptibility to deltamethrin in *An. culicifacies* from Ramnathapuram district, Tamil Nadu [34]. Singh *et al*. (2002) reported 60.4-78.3% mortality in *An. culicifacies* [19]. Sharma *et al*. (2004, 2007) noted 89.4 to 92.5% mortality against deltamethrin in this mosquito species [16, 35]. However, it is still an effective insecticide for the control of mosquito vector [15-20, 34, 36] (Table 1).

3. *Anopheles fluviatilis*

An. fluviatilis is responsible for malaria transmission of about 15% of new cases annually in hilly and foot hill regions of Odisha, Madhya Pradesh, Uttarakhand and Chhattisgarh [37]. As per NVBDCP reports up to 1997, it was resistant to DDT in 11 districts from 8 states [10]. *An. fluviatilis* was found susceptible to DDT in Odisha [22, 35]. But recently from Koderma and Gumla district of Jharkhand, Singh *et al*. [15, 30] reported resistance against DDT in these mosquitoes. *An. fluviatilis* has been found susceptible to malathion and synthetic pyrethroids in most of the studied areas [15, 22, 29, 35].

4. *Anopheles stephensi*

An. stephensi is an important malaria vector in urban areas of India. It has predilection for breeding in man-made breeding places. So IRS is not used for its control in vector control programme in urban areas. However, it has developed resistance to DDT, malathion and dieldrin in many areas of the country [10, 11]. This resistance may be due to use of these insecticides in IRS activity by NVBDCP in rural areas. In Manglore city of Karnataka, it has been found resistant to malathion, but susceptible to DDT and permethrin [38]. Resistance to DDT was reported in Kerala, Rajasthan and Gujarat and Madhya Pradesh [39-41]. Tikar *et al*. (2011) [39] reported a 38.46-100% mortality in *An. stephensi* against malathion and 90-100% mortality against deltamethrin, showing a variable degree of resistance against malathion and deltamethrin. Bansal and Singh [42] however showed 100% susceptibility against synthetic pyrethroids like deltamethrin in Rajasthan.

5. *Anopheles minimus*

An. minimus is the primary vector in north eastern region of India. It is a species complex of three sibling species A, C & E, out of which species A is the main vector in India. Following the application of DDT and other indoor residual insecticides by NVBDCP, *An. minimus* disappeared from Uttar Pradesh and was believed to have also from the north-eastern region; however, it was again discovered transmitting malaria in north eastern region [43]. During the last one decade studies, there are only a few published reports on the susceptibility status of this mosquito species. It has been shown to be highly sensitive to DDT, malathion and deltamethrin as up to 100% mortality with these insecticides has been obtained in Assam and Bihar [44-45]. But recently, in Tripura and Orissa Odisha, tolerance against DDT has developed in this species [46-48].

Table 1: Report on insecticide susceptibility status of malaria vectors in India. (2000-2013)

Species	State	Susceptibility status*			Reference
		Organochlorine (DDT)	**Organophosphate (Malathion)**	**Pyrethroid (Deltamethrin)**	
An. culicifacies	Maharashtra	R	VR	VR	31
		R	VR	S	18
	Chhattisgarh	R	R	R/S	32
		R	VR/R	VR	16
	Madhya Pradesh	R	VR	VR	36
		R	R/S	R/S	33
		R	-	-	21
	Gujarat	R	-	R/S	19
	Jharkhand	R	S	S	30
		R	VR	S	15
	Rajasthan	R	R/S	S	17
	Uttar Pradesh	R	VR	S	20
		R	-	-	23
		R	S	S	25
	Odisha	R	R/S	VR/S	34
		R	S	-	26
		R	R	-	22
	Uttaranchal	-	VR/S	-	29
	Tamil Nadu	R	-	R	24
	Karnataka	-	VR	-	24
An. fluviatilis	Maharashtra	R	VR	VR	31
	Jharkhand	R	S	S	15,30
	Odisha	VR/S	VR/S	S	35
An. stephensi	Gujarat	R	R	VR/S	39
	Rajasthan	R	R/S	VR/S	39
	Karnataka	S	R	VR	38
	Kerala	R	S	S	40
	Madhya Pradesh	R	VR	-	41
An. minimus	Assam	VR	-	S	45
	Tripura	VR	-	S	46
	Odisha	VR	-	S	47
		R	-	S	48
An. annularis	Maharashtra	R	VR	VR	31
	Jharkhand	R	S	S	30
		R	VR	S	15

*As per WHO criterion (Mortality=98–100%: Susceptible; 81–97%: Verification required ;< 80%: Resistant).

6. *Anopheles annularis*

An. Annularis, a secondary malaria vector in certain parts of India, is a complex of two sibling species A and B. It has been found resistant to DDT as well as dieldrin /HCH from most parts of India. Though *An. annularis* is susceptible to malathion, fenitrothion and deltamethrin, Das *et al*. (2000) reported 100% susceptible against DDT in Bihar [45]. However, Singh *et al*. (2010) found 45.9% mortality against DDT in Jharkhand showing resistant to DDT [15], but in both the studies this species was reported to be susceptible to malathion as well as deltamethrin. Recently in Gadchiroli, some tolerance against malathion and deltamethrin has been reported by Singh *et al*. (2012) [31].

The susceptibility status of other malaria vector species *viz*., *An. sundaicus*, *An. dirus*, *An. vruna* and *An. philippinensis* prevalent in the country by and large remain unchanged[11] as there are no reports on insecticide susceptibility status published during the past decade as per our knowledge.

7. Conclusion

Most of the studies revealed that resistance against DDT is prevalent in most of the malaria vector species (Figure 1). Even in *An. minimus*, which was considered to be susceptible to this insecticide, resistance against DDT has started to develop. Bye and large, *An. culicifacies* and *An. stephensi* are resistant to malathion also but resistance against synthetic pyrethroid is developing. *An. fluviatilis*, *An. minimus* and *An. annularis* are more or less susceptible to malathion and deltamethrin. As the chemical molecules available for the role of insecticide are very few and invention of new molecules takes time, this is the need of time that increasing trend of resistance status of mosquitoes against the insecticides used in the vector control programme have to be minimized. In past ten years, researcher's focus on this aspect has been low. There are only a few studies on the susceptibility status of the mosquitoes against various insecticides. So it is the time that emphasis on these studies should be given. Again the appropriate use of the insecticides like rationale use with rotation of insecticides and insecticides combinations can be an effective strategy to combat this insecticide resistance.

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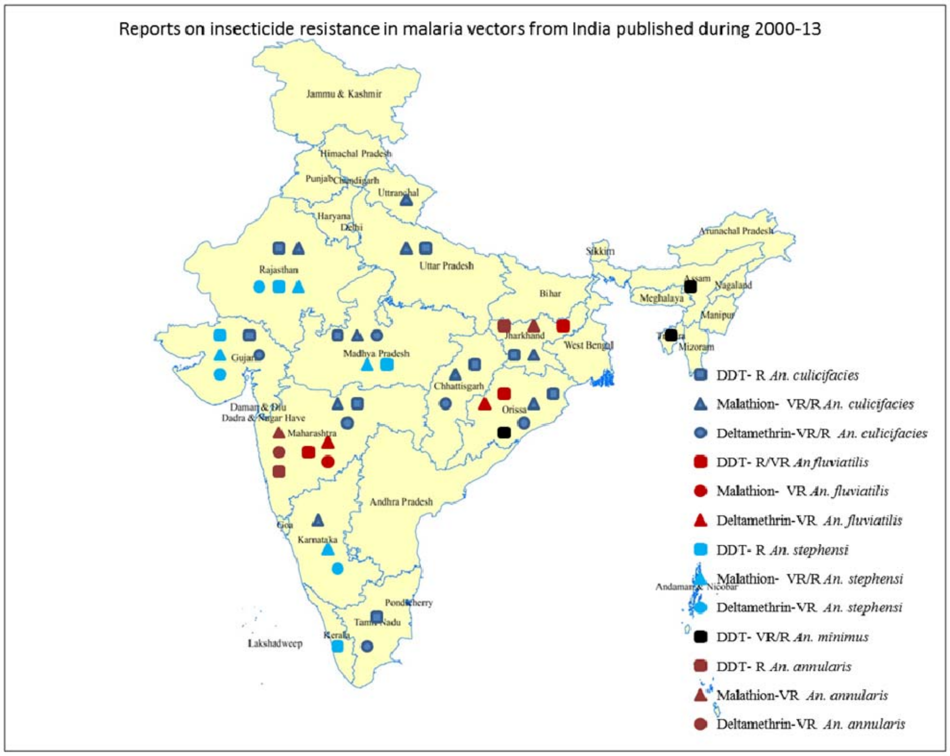

Fig 1: Insecticide susceptibility status of malaria vectors in India

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