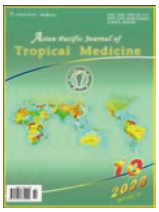

Perspective

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Insecticide resistance in Indian *Anopheles*: A stumbling block for malaria elimination

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Malaria is a mosquito-borne disease caused by protozoan parasites of *Plasmodium* genus, inflicting health of human living in tropical and subtropical regions of the globe since time immemorial. India possesses highly diverged eco-climatic regions and rich biodiversity and is also highly endemic to malaria, contributing to about 87% of total cases in Southeast Asia and about 4% to the global malaria cases[1]. Although African countries contribute majorly to global malaria, malaria in India was considered to be highly complex due to several factors, including distribution of large varieties of species and subspecies of *Anopheles* mosquitoes adapted to different geographic locations[2]. For example, the malaria vector *Anopheles* (*An.*) *culicifacies*, mainly distributed in rural areas, is responsible for transmission of about 65% of total malaria cases and *An. fluviatilis*, distributed mainly in hilly forested areas, contributes to about 17% of total cases in India[3]. Other species distributed locally and focally, *e.g.*, *An. minimus* and *An. baimai* (Northeastern states), *An. sundaicus* (Andaman and Nicobar Island) and *An. stephensi* (urban areas) transmit malaria in their respective confined areas of distribution. Apart from these six primary vectors of malaria, some secondary malaria vectors, *e.g.*, *An. annularis*, *An. subpictus*, *An. philippinensis* and *An. jeyporiensis* also spread malaria to some extent in India[4].

During 1960s, simultaneous usage of dichlorodiphenyltrichloroethane (DDT) as insecticide in controlling malaria vectors and chloroquine as antimalarial treatment had brought down malaria incidences to a significant extent in India. This success, however, has been overshadowed by evolution and spread of resistance to DDT by *Anopheles* mosquitoes and to chloroquine by the malaria parasite *Plasmodium falciparum* at the global level including India. This had led to the World Health Organization and malaria control programs of endemic countries to deploy alternative insecticides and antimalarials. Although Stockholm Convention in 2004 had limited the use of DDT all over the globe in general, India still continues to use DDT for controlling vectors of both malaria and leishmaniasis[5]. While DDT is principally used as indoor residual spray (IRS), other chemicals (organophosphates, carbamate, pyrethroids *etc.*) are also in use for malaria control in India as adulticides[6]. Besides, another vector control method to prevent man-mosquito contact is the use of long lasting insecticide-treated bed net (LLIN) since 2009. In India, usage of IRS and LLINs are determined by annual parasite incidences in defined endemic localities. For example, areas with annual parasite incidences more than two get IRS and areas greater than five get LLINs as adulticides (http://.nvbdcp.gov.in). Although all these vector control measures have proven successful to a larger extent in contributing to decrease in malaria incidences in recent years in India, large scale usage of these chemicals in the field had contributed to emergence of mosquito vectors resistant to almost all the insecticides. A recent over 25 years meta-analysis of data on insecticide-resistant malaria vectors collected in 145 districts of 21 Indian states and two union territories indicates that *An. culicifacies* was resistant to at least one insecticide in 70% of the studied districts, mostly to DDT and malathion, justifying widespread resistance of *An. culicifacies* to multiple insecticides[7]. This, along with challenges in malaria diagnosis[8], widespread prevalence of chloroquine-resistant malaria parasite *Plasmodium falciparum* and artemisinin-resistant parasites knocking the Indian boarder[9] are

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daunting for targeted malaria elimination program by 2030 in India. In the absence of an effective malaria vaccine, constantly changing ecoclimatic factors and rapid urbanization in India creating new foci for vector breeding, and malaria elimination seems to be quite an uphill task.

Insects are considered to be the most successful organisms on earth, as they quickly evolve and efficiently adapt to new environmental conditions. On this line, as a measure of adaptation, *Anopheles* mosquitoes of India have evolved resistance to almost all the insecticides in use for vector control[10]. Considering vector control as the most effective way to malaria control/elimination and no new insecticides are planned for introduction into malaria control program in the near future, novel approaches must be adapted for controlling mosquito vector and thereby contributing to malaria elimination in India. To this respect, integrated vector management by improving efficacy, cost-effectiveness, ecological soundness and sustainability of vector control and introduction of new biological control ways could support the targeted elimination effort. Moreover, alternative methods of vector control, *e.g.*, sustainable release of *Anopheles* mosquitoes incompetent of carrying malaria parasites (with *Wolbachia*-infected and employing gene-editing technologies) in malaria endemic locations could also be effective. Above all, community participation and ownership to different novel vector control measures could be the key to success to malaria elimination in India.

Conflict of interest statement

The authors declare that there is no conflict of interest.

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Authors' contributions

N.K. collected information related to subject and wrote the initial version of the manuscript. A.K.M. helped in preparation of manuscript. A.D. conceptualized the idea and prepared the final version of the manuscript.

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