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A review on the prevalence and susceptibility/resistance status of *Aedes* mosquitoes in Rajasthan

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Abstract
The aedes mosquitoes are efficient vector causing various infectious diseases across the world. Dengue outbreak is a major threat to human health in various provinces of India. Despite of dry season in Rajasthan a very high number of dengue fever cases have recorded. This review emphasized current status of Aedes aegypti mosquitoes abundance, their key breeding habitats and susceptibility to currently applied insecticide measures in order to know the role of vector in transmission of several infectious diseases in northern-west state, Rajasthan. Data highlighted that mostly cases of dengue occurred after the monsoon season. The dengue vector density was found to correlate with rainfall, temperature and relative humidity fluctuations. Due to continuous and unabated use of insecticides in agriculture sector and public health progressively started to selection pressure, inducing rapid development of resistance in mosquitoes vectors. The data related to insecticide susceptibility interpreted and even explored development of resist come up with a background for an understanding to trigger the development of novel tools and alternative strategies to control aedes mosquitoes population concerned with public health.

Keywords: *Aedes aegypti,* dengue, insecticide resistance, susceptibility

1. Introduction

A genus Aedes of mosquitoes is highly invasive in nature and transmit mosquito vector borne viral diseases, in tropical regions to temperate ones across the world [1]. The species Aedes aegypti L. and Aedes albopictus (Skuse) are the main vectors of chikungunya, dengue, zika and other relevant infectious diseases and principally occurred in dengue-endemic countries including India [2]. The main dengue vector, A. aegypti is the major vector that transmit dengue virus and causes about 2/3 cases of infection annually [3]. A. albopictus is primarily belonging to a forest species that has now adapted to rural as well as urban environments. Dengue has become a global threat to human lives affecting more than 100 countries of the world. About 50–128 million new dengue cases infecting more than 3.9 billion people, causing 20,000 deaths yearly [4, 5, 6, 7, 8, 9]. The incidences of dengue have dramatically increased in the last decade around the globe. 30-folds hike in the cases of dengue have seen in the last past five decades [7, 10, 11]. This review has attempted to compile the available data on the seasonal abundance and prevalence at breeding sites, insecticides susceptibility or resistance status of different species of aedes in the Rajasthan.

2. Dengue cases in Rajasthan

The state Rajasthan is one of the dengue endemic provinces in India. Entomological survey on dengue vectors reported outbreaks of dengue virus (DEN-1,2,3,4) in arid and semi-arid districts of Rajasthan [12, 13, 14, 15]. In Jaipur city, the dengue surveillance reported IgM seropositivity highest in the year 2009 and least were recorded in 2011. Most of the cases occurred after the monsoon season, a peak of cases reported in month of October [16, 17]. In 2017, Rajasthan reported 14 deaths due to the dengue fever. In 2018, the state is listed at sixth position where more than 3,000 dengue cases reported till month of September and had 4 deaths due to dengue fever. In the year 2019, number of deaths reached to 12 due to the dengue fever. In 2019, the number of positive cases 7,981 diagnosed so far. In Rajasthan zika virus transmission was also detected due to high prevalence of its vector,A. aegypti.

First laboratory confirmed case of Zika virus disease in Rajasthan was reported in the year 2018 in the Jaipur city [18, 19, 20]. The State Health Department has reported four-lakh mosquito breeding sites after monsoon period, August to November month of the year 2019. This created alarming condition to high spreading rates of the diseases in the state, causing pressure to control the mosquitoes outbreak [19, 21].

3. Seasonal prevalence of A. aegypti

Distribution and seasonality of Aedes mosquitoes predominantly affected the vertical transmission of dengue viruses in arid and semi-arid areas of Rajasthan [22, 23]. A large number of breeding sites of Aedes mosquitoes in urban settings during all the seasons were explored in the desert zone. Water storage habitats in summer season emerged to be the contributing factor of mosquitoes vector abundance in urban zones of arid and semi-arid settings. Seasonal abundance of A. aegypti, A. albopictus and A. vittatus and their intensive role in transovarial transmission has been studied in desert and non-desert districts of Rajasthan [24, 25]. Earlier studies reported that A. vittatus was confined in non-desert zone, Jaipur district only [26]. Temperature about 16 0C and up to 28 0C favored the process of development of larvae of A. aegypti into adults and above 30 0C observed lethal to immatures. A seasonal peak of population of adults of A. aegypti exhibited in favorable local climatic conditions and subsequently led to raise the dengue cases. Aedes mosquitoes were highly adapted domestic container breeder as larval forms were abundantly present in domestic and peridomestic habitats even in plant holes in socioeconomic area of Jodhpur, endemic for dengue in Rajasthan [27, 28, 29]. Higher aedes vector density indengue endemic district Jalore, Rajasthan from 1992 to 1993 was associated with favorable temperature range, relative humidity and pH conditions. The dengue virus strain-3 has been observed to be active in this arid region [30]. In Jaipur district, A. vittatus caused highest infection (20%) of vertically transmitted virus followed by A. albopictus (18.7%) and minimum by A. aegypti during the year 2006 -2007. Ae. albopictus has shown maximum percentage of vertically transmitted virus. High infection rate was explored by A. aegypti mosquito during summer and rainy seasons especially inarid district, Jodhpur and semi arid districts too. The data suggested the tendency of over storage of domestic water by the local population which led into increased mosquito density and vertically active transmission of virus [31]. In Alwar, rich productive breeding sites for A. aegypti were assessed where house index, container index and Breteau index reported to be 58.62, 12.44 and 64.66, respectively. Though, pupal index was observed very high (141.38) [32]. The A. aegypti was observed to be prevalent in all sites of Udaipur. The house container index and breteau index found to be increased after monsoon period. High (8.2%) containers indices were observed in the Rampura area in September 2016 whereas, Pratap Nagar and Tekri area were also recorded to be high in container index and house index for A. aegypti during the same time period [33].

4. Susceptibility/Resistance status of Aedes aegypti

Studies have been carried out by earlier investigators to assess susceptibility status against commonly used insecticides in dengue vectors control programme in different areas of North –West India [34, 35, 36]. Aedes mosquitoes were exposed to various diagnostic doses of organophosphate (Malathion), pyrethroids (deltamethrin, lambda-cyhalothrin, and permethrin) and chlorinated hydrocarbon (DDT) and reported insecticide susceptible in various localities of major districts of Rajasthan [34, 36, 37, 38]. The species Anopheles stephensi, Aedes aegypti and Culex quinquefasciatus,were most prevalent in the arid region of north-western Rajasthan and exhibited susceptibility to four organophosphates (malathion, fenitrothion, fenthion, temephos) and three synthetic pyrethroid (alphamethrin, deltamethrin and fenvalerate) compounds. Temephos was found to be most effective among the tested organophosphates, followed by fenitrothion, fenthion and malathion. Larvae of A. aegypti were reported most susceptible to pyrethroids followed by Cu. Quinque fasciatus and An. stephensi. Among the pyrethroid compounds tested alphamethrin was noted most toxic followed by deltamethrin whereas, fenvalerate showed least toixicity [38]. F1 laboratory reared generation both larvae and adults of A. aegypti were reported susceptible to cypermethrin and permethrin as tested. LC50 and LC90 values for larvae were calculated as 0.0003 and 0.0794 ppm and 0.0063 and 0.0158 ppm to cypermethrin and permethrin, respectively. Adult mortality to discriminating concentrations observed to be LC50 and LC90 to be 0.0019 and 1.0501 ppm and 0.1000 and 0.3981 ppm, respectively [39]. For effective control of mosquitoes vectors, information on their insecticide susceptibility status is much essential [17, 40].

The mosquitoes vector control programme principally still reliant on use of chemical synthetic insecticides to reduce the mosquito's population. Although, insecticides present an effective tool in controlling the emerging mosquito-borne diseases but the development and spreading of insecticide resistance is a major threat to sustainable mosquitoes control [41]. The four classes of insecticides such as organochlorine, organophosphate, pyrethroids and carbamates are primarily applied for adult mosquito control, larval mortality and source reduction. In India indoor residual spraying practiced as the prime method of mosquito vector management which applies approximate on 80 million households and 40% of the population is provided protection [42]. WHO has made recommendation for 12 insecticides for indoor spraying. The main insecticides used for indoor residual spraying include DDT, malathion and synthetic pyrethroids in rural as well urban areas in India and pyrethroids are used for long lasting insecticidal nets (LLINs). The development of protective vaccine, increasing dengue cases and insecticide resistance in aedes vectors have become crucial issue for human health [43].

Continuous indiscriminate use of insecticides has led to arising population of resistant mosquitoes. Not only insects exhibit genetic resistance to a particular class of insecticide and are "selected" to transfer the resistance to coming generations, but also results in development of resistance more rapidly to other insecticides, this is known as cross resistance with the same mode of action. An almost similar term, multiple resistance occurs when that resistance occurred two or more insecticide classes with unlike modes of action [43].

Te Insecticide Resistance Action Committee (IRAC) defines resistance as "the selection of a heritable characteristic in an insect population resulting in the repeated failure of an insecticide product to provide the intended level of control when used as recommended" [44].

Although, insecticide resistance in the vector A. aegypti has been developed around the world and the World Health

Organization (WHO) has been made efforts to control the developing resistance in insects [43]. A population is considered susceptible presenting 98 -100% mortality to the diagnostic dose of insecticide and mortality below to 80% considered as resistant if compare to the susceptible strains [42].

Insect has developed four different resistance mechanisms of insecticide resistance such as:

A. Behavioural resistance, which shows modifications in insect behaviour to avoid the toxic effects of chemical insecticides. The contributing factor to develop the mosquito avoiding behaviors with insecticides is mainly reduced penetration by thickening of the cuticle, modifications in digestive tract linings that limit the chemical insecticides absorption [45].
B. Metabolic resistance, due to an increased detoxification caused by the increased activity of enzymes carboxylesterases, multi-function oxidases (MFOs), and glutathione, P450- monooxygenases, S-transferases (GSTs) involved in the chemical insecticide metabolism [45, 46].
C. Target-site resistance, modification at the target site of action reducing against insecticides, which prevent insecticide binding at the same loci. Mutations in the voltage sensitive sodium channel (Vssc) gene are one of the most common causes of target-site resistance [45, 47].
D. The Knockdown Resistance (kdr), It involves alterations that render lack of sensitivity of acetyl cholinesterase or conformational changes on the voltage-gated sodium gates that inhibit insecticide binding and thus prevents the mosquito from being knocked down after exposure [6, 47].

In Rajasthan, A. aegypti has developed a strong resistance to commonly used chemical insecticides as adulticide and larvicide which needed continuous monitoring of susceptibility for effective vector control programme. Insecticide resistance management (IRM) is crucial to maintain vector control sustainable. A. aegypti, A. vittatus and A. albus were encountered most prevalent species both in rural and urban areas exhibit susceptibility to different concentrations of organophosphate and pyrethroid in three desert districts (Bikaner, Jaisalmer and Jodhpur) and three non-desert districts (Alwar, Ajmer and Jaipur) of Rajasthan. A. aegypti exhibited possible resistance to DDT and dieldrin more pronounced in rural areas as compared to urban areas [37]. DDT and pyrethroid resistance reportedin A. albopictus and absence of knockdown resistance (kdr) mutation [48]. Similarly, insecticide resistance was evaluated in the adult mosquitoes of A. aegypti to cypermethrin and permethrin. Resistance ratio against permethrin (RRLC50=2 and RRLC90=2.5) and cypermethrin (RRLC50= 1.5 and RRLC90= 3.16) was observed in field collected population, as compared to laboratory susceptible population [49]. Elevated GST activity ranged from 0.1186 to 1.722 µmol/mg protein in resistant strain than susceptible strain in A. aegypti from urban province. Alpha esterase activity was 1.5 to 2.7 times higher than susceptible strain. Biochemical resistance mechanism studies will support in critically reviewing for implementing effective vector strategies [50].

Insecticide resistance is a serious emerging problem and the national program has no alternative measures for effective vector control or insecticide resistance management.

5. Conclusion

Hence, the review summarized Aedes mosquitoes vector population interrelated with natural breeding sites and seasonal climatic factors in different zones of Rajasthan. The important highlights on emergences of dengue cases during last years probably contributed by increasing aedes mosquitoes population. Although, chemical insecticides are effective tool among the various control measures in mosquito vector management and cannot be totally neglected. Therefore, monitoring of

susceptibility to insecticides and interpretation of resistance level in aedes vector at times is necessary so that alternative strategies with effective management plan can be designed to prevent the mosquito borne diseases.

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