Indian Journal of Entomology 85(2): 503-513 (2023) DoI. No.: 10.55446/IJE.2022.593

A REVIEW ON VECTOR BORNE DISEASE TRANSMISSION: CURRENT STRATEGIES OF MOSQUITO VECTOR CONTROL

S Manikandan, A Mathivanan, Bhagyashree Bora, P Hemaladkshmi, V Abhisubesh and S Poopathi*

Unit of Microbiology and Immunology, Vector Control Research Centre,
Indian Council of Medical Research, Department of Health Research,
Ministry of Health and Family Welfare, Puducherry 605006, India
*Email: Subbiahpoopathi@rediffmail.com (corresponding author)

ABSTRACT

In this review, the mosquito vector borne diseases (VBD) majorly malaria, dengue, filariasis, chikungunya, Japanese encephalitis, Zika were presented to comprehend the global disease incidence as the control of these disease transmitting vectors are challengeable globally nowadays. It has been found that malaria affects nearly 500 million people and lymphatic filariasis about 100 million people worldwide every year. About 25 million people are infected by dengue, with approximately 25,000 deaths annually. For mosquito larval adult control measures, synthetic pesticides playing major role but owing to resistance development its application is impeded. Alternatively, bacterial biopesticides are very useful for larval control mainly due to environment friendliness and lack of resistance development. As of now, *Bacillus sphaericus* (*Bs*) and *B. thuringiensis israelensis* (*Bti*) are in use but *Bs* is nowadays not recommended for field application due to resistance. Significant results on resistance development are noticed in India, Brazil and France. Due to these situations, there is a growing interest in discovering novel biological agents from natural sources. In the present review, the current global scenario of VBDs were discussed.

Key words: Vector borne disease, mosquito vectors, socio-economic impact, integrated vector management, synthetic insecticides, bio-pesticides, vector control

In public health, the term "vectors" in broad spectrum refers to any organisms which can communicate infectious diseases to mankind and other living organisms. Major vectors belong to insects of the phylum *Arthropoda* in animal kingdom. Some important vectors are mosquitoes, sand flies, ticks, simulium, triatomine bug, etc., which transmit diseases by means of the infected bites. Among these insect vectors, mosquitoes play a vital role in transmitting many dreadful diseases like dengue, filariasis, Japanese encephalitis, chikungunya, malaria, West Nile fever, etc. These vectors are ectothermic and are vulnerable to climatic conditions. Weather affects the abundance, habitat suitability and distribution of the vector population (Dhanasekaran et al., 2014). Besides, it affects the reproduction rates, survival of the vectors, disease spreading capacity, feeding and biting rates. In addition, it also affects the multiplication and survival of the disease-causing pathogens which infests inside the vector. Globally, vectors are responsible for 17% of infections of mankind. More than 3.9 billion in 128 countries are prone to dengue infection with about 96 million dengue cases reported every year. As per latest report from World Health Organization (2022) nearly 0.5 million of severe dengue cases every year. Malaria is one of the major dreadful vector-borne diseases which can cause substantial economic and social disruption. Every year nearly 4,00,000 deaths were recorded due to malaria. Malaria affects mostly children below 5 years of age (WHO, 2018). In addition to the above, other illnesses like American trypanosomiasis, kala-azar and schistosomiasis affect the people worldwide. The burden of these vector borne diseases (VBDs) is highest in tropical and sub-tropical regions due to poor socioeconomic conditions. Most of these vectors are insects that suck blood from the host (animal or human). Vectors ingest the pathogen that causes disease while feeding on the blood of a diseased person and later transmit it to others. Due to the lack of effective vaccines or specific pharmacological drugs for most of these diseases particularly dengue fever and West Nile virus, vector management is the primary key element for the eradication of vector-borne diseases (El-Kersh et al., 20l6). There are four methods to control vectors which include environmental control, chemical control, biological control, and personal protection measures. Biological control is a powerful strategy to reduce public health problems related to vector-borne diseases without affecting the environment (Cuthbert et al., 2018). In other words, biological control is an environment-friendly preventive technique to control pest organisms.

Vector control

During the 20th century, biological control of mosquitoes was very effectively carried out. However, the application of chemical insecticide was in top priority because of the easy availability and cost-effectiveness (Saleeza et al., 2014). However, due to the development of insecticide resistance in these vectors, in addition to their ill-effects on the ecosystem, chemical insecticides were less preferred, and biological control agents were prioritized. Biological control agents include larvivorous fishes (*Gambusia affinis, Poecilia reticulate* and *Clarialfuscus*) dragonflies, damselflies, a mosquito species (*Toxorhynchites*), cyclopoids and copepods. Besides, mosquitocidal bacteria like *Bti* (*Bacillus thuringiensis* var *israelensis*), and *Bs* (*Bacillus sphaericus*) are also used as biological control agents. It is therefore essential to explore further more natural resources and isolate more powerful bio-control agents other than *Bti* and *Bs* for the management of vector populations. Mosquitoes have occupied several natural niches including the greater altitudes, and are ubiquitous, found worldwide (Mondal et al., 2014). These extraordinarily adaptable insects continue to cohabit with humans and their domesticated animals. Even though there is public awareness and knowledge about the importance of these mosquito vectors and their part in causing and spreading disease for decades, VBDs are a significant threat to human society. Rapid urbanization, population dynamics, and industrialization are the main reasons for the increase in the mosquito population and thereby increase in mosquito borne diseases.

Vector surveillance

The study of vectors in relation to their habitats and feeding and resting habits is called vector ecology. Particularly mosquito vectors are more adaptable to climate changes than the other insect vectors. The dispersal, density, and survivability of mosquito vectors depend on biotic and abiotic factors such as competition, predators and humidity, temperature, pH, rainfall, salinity, light/darkness etc. (Chase and Knight, 2003). Furthermore, the ecological factors play a vital role in the occurrence of these diseases either directly or indirectly. More than 3000 species of mosquitoes under 34 genera are found worldwide. Out of these, only 300 mosquito species cause diseases. Mainly, the three mosquito genera of *Anopheles, Culex* and *Aedes* are responsible for spreading most of the dreadful VBDs (Das and Kalyanasundaram, 1989). Vector surveillance of mosquitoes is essential to understand the abiotic and biotic progression that rules abundance and distribution. Throughout their lifecycle, different mosquito species exhibit distinct resting and feeding habits. Most mosquito species rest during the day and are active from dusk to dawn. Most *Anopheles* and *Culex* species bite at night, while *Aedes* and *Armigeres* species feed during the day. The preference of hosts for mosquito blood-feeding differs between humans and other mammals and birds (Patil et al., 2002). Water is the primary breeding source for all mosquito species. Eggs are laid in water, and the developmental stages of larvae and pupae occur in water. Mosquito larvae prefer to live in water. The mosquito habitats are numerous and diverse, such as tree holes, ponds, and lakes. Some mosquito species breed in freshwater, while others are sewage water breeders. Nowadays, due to rapid urbanization and industrial development, mosquito breeding is enhanced to a greater extent. Human modification of the environment increases mosquito breeding sites (Norris, 2004). The primary cause of the rapid uncontrolled multiplication of vectors is the improper water management system (Joshi et al., 2005).

Disease incidence

According to the most recent malaria report, there is 241 million malaria cases in 2020 and there are 227 million cases in 2019. Malaria deaths are expected to reach 6,27,000 in 2020, a 69,000-death increase from the previous year. Disruptions caused by the COVID-19 pandemic may be responsible for approximately two-thirds of these deaths (47,000). The Democratic Republic of the Congo (13.2 percent), Nigeria (31.9 percent), the United Republic of Tanzania (4.1percent), and Mozambique (3.8 percent) accounted for roughly half of all malaria deaths worldwide (WHO, 2021). Seventeen countries and territories are mentioned to have eliminated filarial disease which is a serious health issues including Cook Islands, Cambodia, Egypt, Maldives, Kiribati, Malawi, Niue, Palau, Marshall Islands, Sri Lanka, Togo, Thailand, Tonga, Viet Nam, Vanuatu, Yemen, Wallis, and Futuna. Five more countries have successfully implemented the recommended strategy, stopped mass drug therapy, and are being monitored to ensure that elimination has been achieved. But still, 50 countries need preventive treatment and in ten of those countries, MDA has not been implemented till the end of 2019 (WHO, 2021).

There was an eight-fold increase in dengue cases in the last two decades. Around 0.5 million cases in 2000, 2.40 million in 2010, and 5.20 million in 2019 were reported. The mortality rate from the year 2000 to 2015 varied from 960 to 4032. Children below five years of age were affected mostly. In 2020, dengue affected several countries like Brazil, Nepal, Mauritania, Bangladesh, Indonesia, Cook Islands, India, Ecuador, Maldives, Sri Lanka, Singapore, Mayotte (Fr), Sudan, Timor-Leste, Yemen, and Thailand. Dengue continues to affect Brazil, India, Vietnam, Philippines, prepare dinner Islands, Colombia, Fiji, Kenya, Paraguay, Peru and Reunion islands in 2021 (WHO, 2021).

Major mosquito borne diseases (VBD)

The major VBDs are malaria, dengue, filariasis, chagas disease, leishmaniasis, schistosomiasis, African trypanosomiasis, Japanese encephalitis, yellow fever, and onchocerciasis. These diseases are caused by viruses, bacteria, and parasites which are transmitted by vectors. Every year there are more than 7 lakh deaths reported due to VBDs. In 2014, major outbreaks of malaria, chikungunya, dengue, zika, and yellow fever were reported affecting the lives of many people and, posing a challenge to health systems in many nations. Other VBDs like chikungunya, leishmaniasis, and lymphatic filariasis result in persistent struggling, life-long morbidity, incapacity, and occasional stigmatization (WHO, 2020).

Malaria: Malaria is an acute febrile disease caused by *Plasmodium* species, an intracellular protozoan parasite that is transmitted by the bite of infected *Anopheles* mosquitoes. *Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale* and *Plasmodium malariae* are the common parasite species that cause malaria. In India, *Plasmodium vivax* and *Plasmodium falciparum,* pose the most significant risk. *P. falciparum* is the most lethal malaria parasite and the most common in African continent. Infections with *P. vivax* are common in many countries.The first signs of malaria are headache, fever and chills, generally seen after ten to fifteen days after the infective mosquito bite. The symptoms may be moderate and also difficult to apprehend as malaria. If left untreated, *P. falciparum* malaria can progress to a severe infection known as malignant malaria and cause mortality within a day. In 2020, nearly half of the world's population were exposed to malaria. Some of them faced the problem of disease exposure and suffering severe disease, including pregnant women, newborns, children under the age of five, and HIV/AIDS patients, as well as people with low immunity who migrate to areas with high malaria transmissions, such as migrant workers, nomadic people and travelers (WHO, 2021). In India, totally 50 *Anopheles* species mosquitoes are found, but only ten species are the malarial vectors. The vector species of *Anopheles* are *culicifacies, fluviatilis, stephensi, varuna, sundaicus, Philippines, annularis, balabacensis, minimus,* and *jeyporiensis*. Among these, *An. culicifacies* in urban and *An. stephensi* in rural areas are prevalent in India (Das et al., 1990).

Filariasis: Lymphatic filariasis is a tropical and subtropical parasitic disease that affects people of low socio-economic status. Lymphatic filariasis (LF) is caused by three species of nematodes, namely *Brugia timori, B. malayi,* and *Wuchereria bancrofti* which affects the lymphatic system. The bite of infected mosquitoes transmits lymphatic filariasis. It has been one of the foremost public health issues in Africa, South Asia and also in India (WHO, 2013). Elephantiasis, scrotal swelling, and lymphoedema are the manifestations of the illness, which causes pain, disfigurement and lifelong disability. Patients are physically and mentally disabled, facing social and financial losses, contributing to social stigma and poor economic status. Preventive chemotherapy was required for 859 million people in 50 countries in 2019. As per the recent WHO report, there are more than 15 million people suffering from lymphoedema and 25 million men affected with hydrocele globally. These disease manifestations affect approximately 36 million people (WHO, 2021). It is a chronic disorder that results in social, physical, and economic problems. Globally, nearly 120 million people from 83 countries are affected by filariasis. In India 610 million people living in endemic areas in 20 states were affected by filariasis (Devi et al., 2018). Filariasis may manifest as chronic lymphoedema with swelling of limbs, genitals and scrotal sacs (hydrocele). In India alone, it contributes to 44.3 % of the global filariasis burden (7.44 million by lymphoedema, 12.88 million by hydrocele out of 31.26 million filaraemics) (WHO, 2012). Filariasis elimination strategy program released in 2004 through MDA (mass drug administration) with DEC (diethyl carbamazine) and albendazole was focused by 2015 (Shriram et al., 2014). WHO released the GPELF (Global Programme to Eliminate Lymphatic Filariasis) in 1997 based on the two fundamental ways to eradicate filariasis by using mass drug management and MMDP (WHO, 2013). Neglected Tropical Disease Control Programs (NTDCP) was established in 2012 in London to eliminate many NTDs, including LF by 2020 (London announcement to combat NTDs, 2013). Additionally, numerous NGOs have funded to strengthen NTDs applications. Globally, filariasis has been eliminated in countries including Japan, Taiwan, South Korea, Solomon Islands, and China (Sabesan et al., 2000). Fifty-nine species of mosquito vectors transmit filariasis. Amongst them, the principal vector of parasites is *Culex quinquefasciatus*. It is widely distributed in tropical and sub-tropical countries and is responsible for ninety percent of the whole transmission. The vector species of *Culex* are *quinquefasciatus, pipiens, pallens, molestus, globocoxitus* and *australiens* (Devi and Jauhari, 2004), *Aedes* species include *polynesiensis, Samoans,* and *Poecilious,* and *Anopheles* species of *gambiae, flavirostris,* and *barbirostris. Manonioides* species of *annulifera, uniformis,* and *Indiana* also transmit filarial parasites. All of the above species are distributed in diverse areas and various sources. Increased number of microfilaraemics are found in Bihar, Andhra Pradesh, Tamil Nadu, the coastal region of Odisha, Kerala, and eastern Uttar Pradesh in India. In India, approximately 1.5 million people are exposed to the disease with 1.2 million people suffering from filariasis and 2 million microfilaria carriers (Patil et al., 2002).

Dengue: The causative virus for dengue is transmitted by infected *Aedes*, primarily the *Aedes aegypti,* besides other species (WHO, 2021). Dengue virus belongs to flavivirus group associated with other arboviruses like Japanese encephalitis and yellow fever. Dengue is caused by four types of virus (DENVI, DENV2, DENV3, and DENV 4). All four dengue virus serotypes have a unique host immune response to the infection. Currently, a new serotype of the dengue virus has been isolated in Malaysia in 2013 (Mustafa et al., 2015), which is genetically different from the previous three dengue serotypes (DENVI, DENV3, and DENV4) but slightly analogous with DENV2. After blood feeding of a dengue infected individual, the dengue virus enters and multiplies inside the mid gut of a mosquito. The virus then spreads to salivary glands and is transmitted to other hosts during subsequent blood meal. The extrinsic Incubation Period (EIP) is the time taken for a virus to spread from one host to another. When the ambient temperature is between 20 and 28 degrees, the EIP takes about 8-12 days. Differences in the EIP are influenced by ambient temperature, daily temperature variations, virus genotype, and initial viral concentration (Ye et al., 2015). The infected mosquito can spread the virus throughout its lifespan. Next to malaria, dengue fever is another most dangerous mosquito-borne disease in India. It is most common in cities, rural areas, and semi-urban areas. It can occasionally cause severe hemorrhagic manifestation, which can lead to death. (Viroj et al., 2006). Dengue vectors in India are *Aedes aegypti* and *Aedes albopictus,* and were initially found in Africa, and later spread to India. Dengue epidemics were first reported in Asia, Africa, and the United States in 1779-1780, indicating a remarkable tropical distribution of *Ae aegypti* over the previous 200 years. Due to its domestic breeding behavior and feeding preference on human blood, it is perfectly adapted to urban environments. *Aedes albopictus* is responsible for spreading dengue in rural and semi-urban areas. Each year, approximately 50 million dengue cases are reported in India and 2.5 million people face the threat of acquiring dengue. Dengue may become a more severe problem in the future if urbanization continues unabated unless strict environmental control measures are implemented. (Kwa et al., 2008). The *Aedes* species are the principal dengue vector in tropical and sub-tropical nations, particularly Africa and Asia. *Ae. aegypti* and *Ae. albopictus* pose danger of dengue transmission in Europe (Jensenius et al., 2013). The dengue hemorrhagic fever has been widely known since 1950 and is an emerging and re-emerging mosquito-borne disease. Apart from malaria and filariasis in Africa and Asia, dengue is one of the oldest mosquito-borne diseases. As per the latest WHO report, 390 million humans have been exposed to dengue virus, with 96 million new cases.

Japanese encephalitis (JE): Japanese encephalitis (JE) is a dangerous human disease commonly called Brain fever caused by JE-virus and transmitted through mosquito vectors of *Culex vishnui* and *Culex tritaeniorhynchus* in Asia. JE is caused by a flavivirus similar to that causing West Nile, yellow fever, and dengue. Japanese encephalitis was first recorded in Japan in 1871. During outbreaks, 1 to >10 clinical cases per 100,000 populations were reported from disease-endemic countries. As per the literature review, approximately 13,600 to 20,400 deaths and about 68,000 JE-clinical cases occur every year worldwide. Mostly children are affected by JE and adults have developed immunity due to childhood infection, but anyone of any age can be affected. In India, Japanese encephalitis (JE) is common. JEV is primarily an animal virus, with pigs serving as primary reservoirs. Pigs are infected with JEV transmitted by mosquitoes from birds, specifically egrets and pond herons. Humans are merely accidental hosts and are not intended to transmit the virus. JE cases have been reported on a large scale in Bihar, Uttar Pradesh, and Assam besides Andhra Pradesh and Karnataka. *Culex tritaeniorhynchus* and

Cx. vishnui are JE vectors found in India, accounting for 27 verified and suspected vectors. In India, vectors of JE include *An. subpictus, Cx. epidesmus anhyrcanus, Mansonia annulifera,* and *An. barbirostris* besides *Cx. bitaeniorhynchus, Cx. whitmorei* and *Cx. pseudovishnui, Cx. fuscocephala* and *Cx. gelidus.* JE is prevalent in the north eastern and southern part of India and a small part of Gujarat (WHO, 2021).

Chikungunya: Chikungunya is a VBD spread by the mosquito *Aedes albopictus* (Asian tiger mosquito). This mosquito is also known as the jungle mosquito, more common in semi-urban and rural areas. As a result, a more significant number of cases were reported from rural areas. In 2019, Asia and America were affected by chikungunya outbreaks. Pakistan faced a persistent outbreak and reported 8387 cases, while India suffered 62,000 cases. In America and in the Caribbean, 1,85,000 cases were reported; Brazil accounted for more than 90% of cases in America. Chikungunya outbreaks have also been reported in Yemen (2019), Sudan (2018), and more recently in Cambodia and Chad (2020). In 1952, the first case of chikungunya was reported in Africa and Tanzania. In India, the first outbreak occurred in Kolkata (Calcutta) in 1963. In general, chikungunya is not a fatal disease, but however, in 2005-2006, 200 people died due to a chikungunya outbreak in India, which began in Karnataka, Tamil Nadu, Andhra Pradesh, and Kerala. Many hundreds of cases have been detected in Bhilwara, Rajasthan, Chittorgarh, and Udaipur districts and adjoining areas of Madhya Pradesh and Gujarat following floods and heavy rains in August 2006. In addition, the neighboring country of Sri Lanka was affected. In Kerala, 125 people died due to this disease, with a maximum number of casualties occurring in Cherthala and Alapuzha (WHO, 2021).

Zika: Zika is also a vector-borne viral transmitting disease by *Aedes albopictus, Aed. aegypti, Aed. furcifer, Aed. apicoargenteus, Aed. luteocephalus, Aed. Vitattus* (Foy et al., 2011). The ZIKV is a flavivirus genetically related to the *Spondweni* virus (Hayes et al., 2009; Kuno and Chang, 2007). This disease is a challenge for the developing and developed nations and a significant problem in disease-prevalent countries owing to amplified globalization, urbanization, construction of dams, agricultural intensification, deforestation and global warming. Ignorance still prevails about such important mosquito vectors *(Aedes africanus, Aedes hansilli, Aedes luteocephalus, Aedes albopictus, Aedes aegypti,* etc.) and their role in spreading diseases. After Ebola, WHO has anticipated around 3-4 million infected cases in America by subsequent year across and CDCP (Center for Disease Control and Prevention) have advised to avoid the travel of pregnant women where the ZIKV is circulating as described by WHO (WHO, 2016). On 1st February 2016, the organization has publicized the epidemic of ZIKA as ‘’Public Health Emergency of International Concern” (WHO, 2016).

Socioeconomic impact

The socioeconomic condition of a country has an impact on disease prevalence. Knowledge of vector-borne diseases and health consciousness may aid in disease control. Malaria cases increase in poor households due to low resistance caused by malnutrition. Because of the ignorance of the general public, who are unaware of malaria-related symptoms, prompt therapy is not given to patients who develop severe complications. People are still ignorant about symptoms and treatment of malaria. The government plans and implements measures to control mosquito populations and disease spread. In addition, even though diseases are not under control, the government is running awareness campaigns through the social media. The geographic and ecological profile of a region, combined with the area’s socio economic status, allows the multiplication of mosquito population, which results in VBD episodes. Rapid urbanization, excessive deforestation, insecticide and pesticide use, the progress of new agro-ecosystems, and other factors have influenced the emergence of different vectors and VBDs over the last seven decades. Mosquito species that develop resistance require special and immediate attention (Jagdish, 2003). Chemical control measures directly affect mosquito vectors physiologically, and their continuous usage may alter the vector ecology. Mosquitos have plagued Rajkot for decades, and hundreds of people die each year due to VBDs. Dengue, malaria and recently, chikungunya are found in Rajkot, with malaria being the most common. Controlling the spread of vector-borne diseases has emerged as the most difficult challenge for the local government body. Local governments and private, non-governmental organizations are making enormous efforts to control disease and vectors.

Integrated vector management

Integrated vector management (IVM) is a tool that incorporates both chemical and non-chemical approaches and environmental management. It is part of a larger strategy that includes coordination with health division and other divisions, advocacy, social mobilization, educational movements, solid evidence-based choice making, and capacity building. IVM can simultaneously control diseases spreading through various vectors in a specific area or can be a single tool controlling multiple VBDs transmitted by a vector (Grepin et al., 2008). The IVM agenda was utilized in 2004 to control all VBDs and is regarded as a sound method for vector control. Mosquito control must be based on a fundamental understanding of the target species ecology, bionomics, behavior and its relationship to its host and environment. Control measures can be directed at either the immature or adult stages or both stages simultaneously. In general, larval control measures are preferred when adulticidal steps are either expensive or unacceptable to society, and the larval breeding source is limited to a small area. In locations where outbreaks of VBDs are reported often, larval control measures are preferred, and in situations where house spraying alone or in combination with drug administration fails to interrupt disease transmission for technical or operational reasons.

Synthetic insecticides have been used successfully for decades for destroying vector insects in order to control VBDs. Larvicides are necessary weapons that humans have developed to combat larval and adult mosquitos. Many simple and complex synthetic insecticides have been developed due to the advancement of applied chemistry. Insecticides and larvicides are available in the form of dust, powder, or liquid and have different effects on insects. The discovery of DDT (Dichloro-diphenyl-trichloroethane) was a watershed moment in developing modern synthetic insecticides. DDT's contact action against insects was discovered by Muller in 1939. Following the failure of the chemical insecticide control, successive insecticide changes were made, resulting in sequential insecticide selection pressure. Finally, multiple insecticide resistance was developed by mosquito vectors. Mosquitoes that breed in pre-domestic breeding sites are becoming resistant to the various insecticides that protect the crop. Despite using chemical insecticides, these diseases still exist and spread to epidemic proportions. As a result, efforts have been made to find and develop alternative methods for controlling vector mosquitoes to reduce reliance on chemical insecticides. The development of resistance is expected to directly and profoundly impact the re-emergence of these diseases, and disease control may be jeopardized (Jones et al., 1998). Table 1 depicts the comparative analysis on the advantages and disadvantages of synthetic and biological pesticides.

Resistance to insecticides

Mosquitoes pose a severe threat to society by serving as a vector for various dangerous illnesses. Mosquito control programs rely heavily on the regular use of chemical insecticides, which leads to resistance among vectors and environmental hazards, bio-magnification, and adverse effect on public and animal welfare around the world. The global threat of vector-borne diseases and their negative impacts emphasizes the necessity for effective control of mosquitoes. As a result, there is an urgent need to develop new products that have the added benefits of being economic, biodegradable, environment-friendly, and safe to non-target organisms. The current knowledge regarding the plant-derived compounds with larvicidal properties is beneficial in controlling mosquitoes. The molecular mode of action of allele-chemical compounds synthesized from various kinds of plant species and also its secondary metabolites, extracts, and plant essential oils can be used for mosquito control (Senthilnathan, 2020). Since the use of chemical insecticide has become difficult because of bio-amplification of food materials, contamination of food chain, and negative impact on insects with beneficial properties, a surge in biological agents for mosquito control has developed in recent years. Biocontrol agents minimize environmental problems and are the best alternative for chemical pesticides.

Biological pest control

Presently, there is a surge in the use of biological pest control as a potential method for controlling vector mosquitoes. Many mosquitocidal bio-control strategies were evaluated, including their effectiveness, safety to non-targets, and the environment. Some types of protozoa, bacteria, nematodes, viruses, fungi, fish and invertebrate predators have been studied, in order to be used as potential vector control agents. Several bacteria are studied and are found to be effective biological control agents, including *Bacillus thuringiensis morrisoni, Bacillus thuringiensis. jegathesan, Bacillus thuringiensis niedellin, Bacillus thuringiensis canadensis, Bacillus thuringiensis malaysiensis, Asticcacaulis excentricus, Clostridium bifermentans malaysia* and *Synechococcus* (Poopathi et al., 2004).

Among various bio-control agents of *Bacillus* species, two strains of *Bacillus thuringiensis* subspecies *israelensis* and *Bacillus sphaericus* and have been extensively recommended because of their highly potent mosquitocidal activity. More *Bacillus* species like *Bacillus cereus* (Poopathi et al., 2013), *Bacillus alvei,*

Table 1. Control of mosquito vectors using the larvivorous fishes, synthetic and biological pesticides

Insecticides	Advantages	Disadvantages
Synthetic insecticides Malathion Chlorpyrifos Pyrethrins Cypermethrin Permethrin	Effectively used for insect control. Highly active. Effective in mode of action. Long residual activity.	Rapid development of resistance. Environmental pollution. Bio amplification. Harmful to non-target organisms.
Biological pesticides *Bacillus sphaericus* (*Bs*) *Bacillus thuringiensis* subsp. *israelensis* (*Bti*)	Environmental safety. Pollution free. Non-toxic to non-target organism. Recyclable. Effective in minimum dose.	High level resistance to *Bacillus sphaericus*.
Larvivorous fishes *Gambusia affinis* *Poecilla reticulate* (guppy) *Aplocheilus panchax* *Cyanolebias bellotii* (argentine pearl fish) *Oreochromis mossambicus* *Cyprinus carpio*	Self-perpetuating larval control method. Cost-effective. Effective method	It cannot be used in low density of water bodies. Time consuming method, no rapid results possible. It cannot work in water bodies with high vegetation and floating grarbages. Special care needed for transportation and stocking.

Bacillus brevis, *Brevibacillus leterosporous*, *Bacillus circulans, Bacillus subtilis*, *Clostridium bifermentans*, *Bacillus amyloliquefaciens*, *Pseudomonas fluorescens*, and *Pseudomonas aeruginosa* have also been used to control mosquito vectors (Lalithambika et al., 2016).

***B. thuringiensis* subsp. *israelensis* (*Bti*) and *Bacillus sphaericus (Bs)*:** *Bacillus thuringiensis (Bt)*-an entomo-pathogenic bacterium is a rod-shaped, gram-positive, spore-forming bacteria (Abo-Bakr et al., 2020), about 0.5-1.0 x 5μm in size, widely distributed in the natural environment like water, soil, plant leaves, stored grains, insect cadavers, and excreta of arid-birds etc (Poopathi et al., 2014). The mosquitocidal property of *Bacillus thuringiensis* is due to a toxic substance present in parasporal inclusion and crystals produced during sporulation. These toxins comprise of six major proteins aggregated into a solid crystal structure in the bacterial cell. The toxins responsible for the mosquitocidal activity are produced by Cry 4B (135 kDa), Cry4A (125 kDa), Cry11A (68kDa) and CytlAa (28kDa) present in the inclusions. Besides these bacterial toxins as mentioned above, other toxic proteins such as Cryl0A and Cyt2Ba also included. *Bacillus sphaericus* produces binary toxins, which are responsible for the toxic effects to the mosquitoes. The two components of the toxins are Bin B (51 kDa) and Bin A (42kDa), which binds to the specific midgut receptors on the epithelial cells and gastric caecum of the alimentary canal of the mosquito larvae. As like, the other potential strain of *Bacillus sphaericus*, is also gram-positive, rod-shaped, spore-forming bacteria isolated from natural soil. The first strain of *Bs* showing larval toxicity was reported in 1965. Following that, more than 300 strains from worldwide were isolated and identified. Since the late 1980s, *Bs* was used to control *Culex pipiens, Cx. quinquefasciatus* and *Cx. pipiens pipiens* larvae, besides *Anopheles* spp. The advantages of this mosquitocidal strain included high specificity, safe to the environment, potent efficacy, extended activity for a prolonged period of time. As on date, a few potential *B. sphaericus*-2362 based biopesticides are available in the market. The VectoLex and Spherimos are commercialized in the United States and Europe. *B. sphaericus*-1593 based biopesticide (Biocide-S) is also commercialized in India. Similarly, *B. sphaericus*-C3-41 is accessible in the People's Republic of China. All these commercially available bio-pesticides are effective due to specific toxins present in the spores, and these parasporal crystal proteins are directly involved in the mosquito-killing effect. It was reported that *B. sphaericus* has two significant polypeptides namely, Bin-A (42 kDa) and Bin-B (51 kDa), which are responsible for larval toxicity. The mode of action of the toxin complex is associated with the affinity of these toxins to a specialized receptor present in the mid-gut of the larvae of susceptible mosquitoes. The two crystal components work in tandem; the Bin-B component is first binds in affinity with receptors, whereas the Bin-A comprising of 42kDa protein starts binding immediately after Bin-A (51kDa). More than 180 *Bs* strains were tested on a wide range of mosquito species, and the H5a5b serotype was found to be the most potent. Electron microscopy was used to observe the difference in the growth pattern of bacteria cultured from the liquid culture medium. During bacterial growth, vegetative cells started multiplication in the culture medium, and it steadily reached the sporulation stage after the lag phase of several hours. By about 72 hours, the crystal toxins became clear and conspicuous in the spores and the spores started rupturing as a result the crystal toxins were released into the culture medium (Charles et al., 1996). The authors further reported two types of bacterial toxins, namely, crystal and Mtx toxins, and both were entirely different in structural arrangement and synthesizing time. It is clear that the crystal toxins are responsible for the potent larvicidal effect of *Bs* strains and these toxins consists of 51 kDa and 42 kDa polypeptides (Bin-B and Bin-A found in the chromosome) and the components of these two polypeptides are quite different from that of other toxins, such as *Bti*. In spite of the valued nature of the above toxins from *B. sphaericus*, it is very unfortunate that the mosquito larvae developed resistance to the bacteria because of its continuous application over a period of time (Georghiou and Wirth 1997). This serious issue of resistance is mentioned in the succeeding section.

Mode of action of *Bacillus sphaericus:* Mosquito larvae present in the water habitats consume the crystal toxins of *Bs* strains. The crystal toxins are solubilized in the mid gut epithelium and activated by enzymes. Finally, the toxins get bind with epithelial cells, and takes at the stage of death. The whole mechanism on the mode of action of bacterial toxin is narrated as (i) bacterial binary toxins with spores engulfed into the alimentary canal, (ii) dissolving of binary toxin in the significant seat of digestion, *i.e.,* the mid gut, (iii) inactivated protoxin gets activated by the gut enzyme, namely proteases, thereby, the Bin-B and Bin-A (51 and 42 kDa) toxins are activated and cleaved into 43 and 39 kDa proteins (iv) the activated cleaved toxins starts binding to the seat of receptors present on the midgut epithelial cells containing the brush border membrane (MBBM). However, except for some reports on cyto pathological action caused by the toxins, the activity of binary toxin in cells has not been apparent. Significantly, molecular mode of action of binary toxins of *B. sphaericus* in the mid gut of *Cx. quinquefasciatus* was investigated using air-dried mosquito samples, which were easier to preserve and transport from the field to the laboratory (Poopathi et al., 2002).

Resistance to *B. sphaericus:* Previously, it was thought that using a microbial larvicide derived from *B. sphaericus* would not result in mosquito resistance. Nonetheless, previous three-decade studies have shown that the binary toxins from *B. sphaericus* are also complicated in this problem of resistance. The larvae developed resistance to the binary toxin of *B. sphaericus* under continuous application of selection pressure in the laboratory. It has been proved that both in the laboratory and the field experiments, the larvae of *Culex quinquefasciatus* developed resistance to Bin toxin (*B. sphaericus*) as described by (Poopathi et al., 1999). Cross-resistance is also inevitable to some bacterial strains. For example, the laboratory-reared *Culex* larvae already developed resistance to *B. sphaericus.* Resistance inherited to the most potential strain of *B. sphaericus* proved cross-resistance comparatively to other bacterial strains of the similar species of toxin synthesizing organisms, according to laboratory strains. (Nielsen-LeRoux, et al., 2001). As a result, resistance to *B. sphaericus* Bin toxin affects the continuation of already planned vector control programs using this *Bs* strain. Studies on resistance to *Bacillus sphaericus* binary toxins have been undertaken by researchers. It involves modification of receptor, which results in toxin binding affinity changes (Nielsen-LeRoux et al., 1995). As a result, a thorough understanding of the various genetic factors leading to insect resistance to *Bacillus sphaericus* will be helpful in planning strategies for management of resistance. The recent reports confirm an increase in mosquito resistance to these biocontrol agents. Hence, it is essential and indispensable to find newer alternatives to the existing, target-specific ones with high efficacy.

Genetic diversity

It has been noted that only little effort has been put into isolating genetically diverse bacteria, which show a high level of toxicity against insect vectors to be used for mosquito control (Poopathi et al., 2013). There is always a demand for more promising and potential bacterial strains in the production of biological pesticides. In the development of a formulation for medical and agricultural applications, genetically heterogeneous groups of strains can be utilized. The lack of attention paid to the genetically diverse microbes for biological control approach has been considered in recent years.

It is essential to know the spatiotemporal distribution and population dynamics of *Aedes* vectors for the prevention of dengue, especially while planning for dengue control programs. For long-term vector surveillance, an ovitrap surveillance system is an alternative tool. Ovitrap is a user-friendly and effective tool for monitoring dengue vectors and is applied in various countries like Singapore, Australia, Indonesia (Sasmita et al., 2021). A lethal oviposition trap was used to attract gravid female mosquitoes, subsequently laying eggs. Eventually, mosquitoes twig on the substratum. Many such ovitraps have been reported earlier, such as autocidal gravid ovitrap (AGO), sticky trap (ST), double sticky trap (DST) and gravid *Aedes* trap (GAT), Attractive baited lethal ovitrap (ALOT) (Facchinelli et al., 2007; Chadee et al., 2010; Mackay et al., 2013; Eiras et al., 2014; Paz-Soldan et al., 2016).

CONCLUSIONS

Mosquito control is the most important public health objective as mosquitoes transmit many human diseases meticulously, viz., filariasis, malaria, dengue, yellow fever, West Nile, Japanese encephalitis, and Chikungunya. These diseases pose a major problem in disease-prevalent countries and are presently on the rise owing to amplified globalization, urbanization, and global warming. On the whole, the successful method of reducing the occurrence of these human infections is through the control of disease transmitting vector mosquitoes, principally by the application of bio-pesticides to their breeding sites. *Bacillus sphaericus (Bs)*, *Bacillus thuringiensis* var. *israelensis* (*Bti*) are known mosquitocidal bacteria which produce endotoxins for mosquitocidal activity. Regrettably, the development of high and low level of resistance to *Bs* and *Bti*, respectively in several countries has impeded the progress of its application in mosquito control. Under these circumstances, new bacterial isolates have been successfully achieved recently and recommended the future researchers to identify further more suitable methods in vector control program.

ACKNOWLEDGEMENTS

Authors acknowledge the Director, ICMR-Vector Control Research Centre, Pondicherry for proving the facilities. The first author acknowledges the Pondicherry University for granting the NON-NET Fellowship for three years (PU/Aca/Aca-6/1/Ph.D.Fellow.VCRC-2019-20/07).

REFERENCES

Abo-Bakr A, Fahmy E M, Badawy F, Abd El-latif A O, Moussa S. 2020. Isolation and characterization of the local entomopathogenic bacterium, *Bacillus thuringiensis* isolates from different Egyptian soils. Egyptian Journal of Biological Pest Control 30: 1-9.

Chadee D D, Ritchie S A. 2010. Efficacy of sticky and standard ovitraps for *Aedes aegypti* in Trinidad, West Indies. Journal of Vector Ecology 35(2): 395-400.

Charles J F, Nielson-LeRoux C, Delecluse A. 1996. *Bacillus sphaericus* toxins: molecular biology and mode of action. Annual Review of Entomology 41(1): 451-472.

Chase J M, Knight T M. 2003. Drought-induced mosquito outbreaks in wetlands. Ecology Letters 6: 1017-1024.

Cuthbert R N, Jaimie T A D, Amanda C. 2018. Interspecific variation, habitat complexity and ovipositional responses modulate the efficacy of cyclopoid copepods in disease vector control. Biological Control 121: 80-87.

Das P K, Gunasekaran K, Sahu S S, Sadanandane C, Jambulingam P. 1990. Seasonal prevalence and resting behaviour of malaria vectors in Koraput district, Orissa. Indian Journal of Malariology 27(3): 173-181.

Das P K, Kalyanasundaram M A. 1989. Module for chemical control of mosquito vectors: miscellaneous publication, V.C.R.C. (11). Vector Control Research Centre, Pondicherry: 1-39.

Devi N P, Jauhari R K. 2004. Altitudinal distribution of mosquitoes in mountainous area of Garhwal region: Part-I. Journal of Vector Borne Diseases 41(1/2):17.

Devi R R, Raju V. 2018. Information technology in morbidity management of human lymphatic filariasis—A promising tool in global programme for elimination of lymphatic filariasis. Journal of Vector Borne Diseases 55(1): 20.

Dhanasekaran D, Thangaraj R. 2014. Microbial secondary metabolites are an alternative approach against insect vector to prevent zoonotic diseases. Asian Pacific Journal of Tropical Disease 4(4): 253-261.

Eiras A E, Buhagiar T S, Ritchie S A. 2014. Development of the gravid *Aedes* trap for the capture of adult female container–exploiting mosquitoes (*Diptera: Culicidae*). Journal of Medical Entomology 51(1): 200-209.

El-Kersh T A, Ahme, A M, Al-Sheikh Y A, Tripet F, Ibrahim M S, Metwalli A. A. 2016. Isolation and characterization of native *Bacillus thuringiensis* strains from Saudi Arabia with enhanced larvicidal toxicity against the mosquito vector Anopheles gambiae. Parasites & vectors 9(1): 1-14.

Facchinelli L, Valerio L, Pombi M, Reiter P, Constantine C, Della Torre A. 2007. Development of a novel sticky trap for container-breeding mosquitoes and evaluation of its sampling properties to monitor urban populations of *Aedes albopictus*. Medical and Veterinary Entomology 21(2): 183-195.

Foy B D, Kobylinski K C, Foy J L C, Blitvich B J, da Rosa A T, Haddow A D, Tesh R B. 2011. Probable non–vector-borne transmission of Zika virus, Colorado, USA. Emerging infectious diseases 17(5): 880.

Georghiou G P, Wirth M C. 1997. Influence of exposure to single versus multiple toxins of *Bacillus thuringiensis* subsp. *israelensis* on development of resistance in the mosquito *Culex quinquefasciatus* (Diptera: Culicidae). Applied and Environmental Microbiology 63(3): 1095-1101.

Grepin K A, Reich M R. 2008. Conceptualizing integration: a framework for analysis applied to neglected tropical disease control partnerships. PLoS Neglected Tropical Diseases 2(4): e174.

Hayes E B. 2009. Zika virus outside Africa. Emerging Infectious Diseases 15(9): 1347.

Jagdish K. 2003. An inventory of *Culicidae* diversity in Haryana state. Journal of Vector Borne Diseases 40: 112-114.

Jensenius M, Han P V, Schlagenhauf P, Schwartz E, Parola P, Castelli F. 2013. Acute and potentially life-threatening tropical diseases in western travelers—a GeoSentinel multicenter study, 1996–2011. The American Journal of Tropical Medicine and Hygiene 88(2): 397.

Jones D, Elloso M M, Showe L, Williams D, Trinchieri G, Scott P. 1998. Differential regulation of the interleukin-12 receptor during the innate immune response to Leishmania major. Infection and immunity 66(8): 3818-3824.

Joshi V, Sharma R C, Singhi M, Singh H, Sharma K, Sharma Y, Adha S. 2005. Entomological studies on malaria in irrigated and non-irrigated areas of Thar desert, Rajasthan, India. Journal of Vector Borne Diseases 42(1): 25.

Kuno G, Chang G J. 2007. Full-length sequencing and genomic characterization of Bagaza, Kedougou and Zika viruses. Archives of Virology 152(4): 687-696.

Kwa B H. 2008. Environmental change, development and vector borne disease: Malaysia's experience with filariasis, scrub typhus and dengue. Environment, Development and Sustainability 10(2): 209-217.

Lalithambika B, Vani C. 2016. *Pseudomonas aeruginosa* KUN2, extracellular toxins-A potential source for the control of dengue vector. Journal of Vector Borne Diseases 53(2): 105.

Mackay A J, Amador M, Barrera R. 2013. An improved autocidal gravid ovitrap for the control and surveillance of *Aedes aegypti*. Parasites and Vectors 6(1): 1-13.

Mondal R, Devi N P, Jauhari R K. 2014. Occurrence of *Aedes* mosquitoes (Diptera: Culicidae) in urban areas of doon valley, (Uttarakhand), INDIA. Modern Parasitology 28: 255-262.

Muller P K. 1939. Britannica, The Editors of Encyclopaedia. "Paul Hermann Müller". Encyclopedia Britannica, 8 Jan. 2022, https://www.britannica.com/biography/Paul-Hermann-Muller. Accessed 10 March 2022.

Mustafa M S, Rasotgi V, Jain S, Gupta V J M J A F I. 2015. Discovery of fifth serotype of dengue virus (DENV-5): A new public health dilemma in dengue control. Medical Journal Armed Forces India 71(1): 67-70.

Nielsen-LeRoux C, Charles J F, Thiery I, Georghiou G P. 1995. Resistance in a laboratory population of *Culex quinquefasciatus* (*Diptera: Culicidae*) to *Bacillus sphaericus* binary toxin is due to a change in the receptor on midgut brush-border membranes. European Journal Biochemistry 228: 206-210.

Nielsen-Leroux C, Pasquier F, Charles J F, SinÈGre G, Gaven B, Pasteur N. 1997. Resistance to *Bacillus sphaericus* involves different mechanisms in *Culex pipiens* (Diptera: Culicidae) larvae. Journal of Medical entomology 34(3):321-327.

Nielsen-LeRoux C, Rao D R, Murphy J R, Carron A, Mani T R, Hamon S, Mulla M S. 2001. Various levels of cross-resistance to *Bacillus sphaericus* strains in *Culex pipiens* (*Diptera: Culicidae*) colonies resistant to *B. sphaericus* strain 2362. Applied and Environmental Microbiology 67(11): 5049-5054.

Norris D E. 2004. Mosquito-borne diseases as a consequence of land use change. Eco Health 1(1): 19-24.

Patil A V, Somasundaram K V, Goyal R C. 2002. Current health scenario in rural India. Australian Journal of Rural Health 10(2): 129-135.

Paz-Soldan V A, Yukich J, Soonthorndhada A, Giron M, Apperson C S, Ponnusamy L, Wesson D M. 2016. Design and testing of novel lethal ovitrap to reduce populations of *Aedes* mosquitoes: community-based participatory research between industry, academia and communities in Peru and Thailand. PLoS One 11(8): e0160386.

Poopathi S, Mani C, Rajeswari G. 2013. Potential of sugarcane bagasse (agro-industrial waste) for the production of *Bacillus thuringiensis israelensis*. Tropical Biomedicine 30(3): 504-515.

Poopathi S, Mani C, Vignesh V, Lakshmi Praba V, Thirugnanasambantham K. 2013. Genotypic diversity among newly isolated mosquitocidal bacteria (*Bacillus sphaericus*, *B. thuringiensis*, and *B. cereus*). Applied Biochemistry and Biotechnology 171 (8): 2233-2246.

Poopathi S, Mani T R, Rao D R, Baskaran G, Kabilan L. 1999. Cross-resistance to *Bacillus sphaericus* strains in *Culex quinquefasciatus* resistant to *B. sphaericus* 1593M. The Southeast Asian Journal of Tropical Medicine and Public Health 30(3): 477-481.

Poopathi S, Thirugnanasambantham K, Mani C, Ragul K, Sundarapandian S M. 2014. Isolation of mosquitocidal bacteria (*Bacillus thuringiensis*, *B. sphaericus* and *B. cereus*) from the excreta of arid birds. Indian Journal of Experimental Biology 52: 739-747.

Poopathi S, Tyagi B K. 2002. Studies on *Bacillus sphaericus* toxicity-related resistance development and biology in the filariasis vector, *Culex quinquefasciatus* (*Diptera: Culicidae*) from South India. Applied Entomology and Zoology 37(3): 365-371.

Poopathi S, Tyagi B K. 2004. Mosquitocidal toxins of spore forming bacteria: recent advancement. African Journal of Biotechnology 3(12): 643-650.

Rao D R, Mani T R, Rajendran R, Joseph A S, Gajanana A, Reuben R. 1995. Development of a high level of resistance to *Bacillus sphaericus* in a field population of *Culex quinquefasciatus* from Kochi, India. Journal of the American Mosquito Control Association-Mosquito News 11(1): 1-5.

Sabesan S, Palaniyandi M, Das P K, Michael E. 2000. Mapping of lymphatic filariasis in India. Annals of Tropical Medicine and Parasitology 94(6): 591-606.

Saleeza R, Norma-Rashid Y, Azirun M. 2014. Guppies as predators of common mosquito larvae in Malaysia. The Southeast Asian Journal of Tropical Medicine and Public Health 45: 299-308.

Sasmita H I, Neoh K B, Yusmalinar S, Anggraeni T, Chang N T, Bong L J, Tu W C. 2021. Ovitrap surveillance of dengue vector mosquitoes in Bandung City, West Java Province, Indonesia. PLoS Neglected Tropical Diseases 15(10): e0009896.

Senthilnathan S. 2020. A review of resistance mechanisms of synthetic insecticides and botanicals, phytochemicals, and essential oils as alternative larvicidal agents against mosquitoes. Frontiers in Physiology 1591.

Shriram A N, Krishnamoorthy K, Sivan A, Saha B P, Kumaraswami V, Vijayachari P. 2014. Impact of MDA and the prospects of elimination of the lone focus of diurnally sub periodic lymphatic filariasis in Nicobar Islands, India. Acta Tropica 133: 93-97.

Silva-Filha M H, Regis L, Nielsen-LeRoux C, Charles J F. 1995. Low-level resistance to *Bacillus sphaericus* in a field-treated population of *Culex quinquefasciatus* (*Diptera: Culicidae*). Journal of Economic Entomology 88(3): 525-530

Viroj W. 2006. A study on functional similarity between Dengue nonstructural protein 1 and platelet integrin/adhesin protein, CD61.

Wirth M C, Walton W E, Federici B A. 2010. Evolution of resistance to the *Bacillus sphaericus* Bin toxin is phenotypically masked by combination with the mosquitocidal proteins of *Bacillus* *thuringiensis* subspecies *israelensis*. Environmental microbiology 12(5): 1154-1160.

World Health Organization. 2012. Lymphatic filariasis / Fact sheet 2012. https://www.who.int/health-topics/lymphatic-filariasis.

World Health Organization. 2013. Lymphatic filariasis: a handbook of practical entomology for national lymphatic filariasis elimination programmes. https://apps.who.int/iris/bitstream/handle/10665/87989/9789241505642.

World Health Organization. 2016. WHO statement on the first meeting of the International Health Regulations 2005 (IHR 2005). Emergency Committee on Zika virus and observed increase in neurological disorders and neonatal malformations. https://www.who.int/news/item.

World Health Organization. 2018. World health statistics 2018: monitoring health for the SDGs, sustainable development goals. https://www.who.int/docs/default-source/gho-documents/world-health-statistic-reports/6-june-18108-world-health-statistics-2018.

World Health Organization. 2020. Vector Borne Diseases. https://www.who.int/news-room/fact-sheets/detail/vector-borne-diseases.

World Health Organization. 2021. Chikungunya/ fact sheet 2021. https://www.who.int/news-room/fact-sheets/detail/chikungunya

World Health Organization. 2022. Dengue / Fact sheet 2022. https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue.

World Health Organization. 2021. Dengue / Fact sheet 2021. https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue.

World Health Organization. 2021. Japanese Encephalitis / Fact sheet 2021. https://www.who.int/news-room/fact-sheets/detail/japanese-encephalitis.

World Health Organization. 2021. Lymphatic filariasis / Fact sheet 2021. https://www.who.int/news-room/fact-sheets/detail/lymphatic-filariasis

World Health Organization. 2021. Malaria / Fact sheet 2021. https://www.who.int/news-room/fact-sheets/detail/malaria.

Ye Y H, Carrasco A M, Frentiu F D, Chenoweth S F, Beebe N W, van den Hurk A F, McGraw E A. 2015. *Wolbachia* reduces the transmission potential of dengue-infected *Aedes aegypti*. PLoS Neglected Tropical Diseases 9(6): e0003894.

(Manuscript Received: March, 2022; Revised: May, 2022;
Accepted: May, 2022; Online Published: June, 2022)
Online First in www.entosocindia.org and indianentomology.org Ref. No. e22410