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Mosquito-borne diseases, their impacts and mosquito vector control methods - A review

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Abstract

Vector borne diseases are increasing nowadays and can spread to new locations easily. Diseases like zika virus fever, West Nile fever, malaria, yellow fever, Japanese encephalitis, dengue, etc. are examples of mosquito-borne diseases. These diseases are majorly caused by three species of mosquitoes *Anopheles, Aedes*, and *Culex*. Most mosquito vector control methods depend upon outdoor spraying, impregnated nets, or indoor residual spraying of chemical insecticides and it was observed that many mosquito species evolved resistance to major pesticide classes. The disadvantages of using chemical pesticides are the development of resistance in mosquitoes and also the harm it causes to other non-target organisms, in addition to the higher cost, more labor, and other drawbacks. Using DEET is also not as preferable as it can induce muscle twitching, seizures, slurred speech, nausea, and rashes. DEET will not give long-term protection against all malaria-causing mosquito species, such as *Anopheles*. Whereas biocontrol agents used for mosquito control show no environmental pollution or resistance. *Bacillus thuringiensis israelensis* and *Bacillus sphaericus* biopesticides tend to remain longer in the environment, particularly in dirty water, and hence may be a viable choice for long-term mosquito control. They have the least adverse effect on living things like humans, domestic animals, and wildlife.

Keywords: Mosquito-borne diseases; *Anopheles*; *Aedes*; *Culex*; Biological control and vector; Fever

1 Introduction

Emerging and re-emerging diseases spread by vectors are a major public health concern across the world [1]. In the last two decades, several of these diseases have emerged at an increasing rate, and have spread to new areas [2]. Vector-borne diseases are on the rise, causing new infectious diseases which are mainly caused by viruses. Zika virus fever, Malaria, dengue, yellow fever, Japanese encephalitis, chikungunya, and Rift Valley fever are examples of mosquito-borne diseases. These deadly diseases have been a major health concern across the world [3].

In the last two decades, some vector-borne infections have colonized new areas, and also an equal number of endemic diseases have seen a rise in occurrence. Humans have long been subjected to the devastating effects of vector-borne infectious diseases [4]. For example, Malaria and dengue are extremely dangerous vector-borne diseases and during 2017 they caused around 6, 20,000 and 40,500 fatalities respectively, predominantly in continents like Africa as well as Asia.

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1.1 Malaria

Malaria is a parasitic disease spread by the female *Anopheles* mosquito. *Plasmodium vivax, Plasmodium falciparum, Plasmodium malariae, Plasmodium ovale,* and *Plasmodium knowlesi* are the major malarial parasites [5]. In the 2018 World Malaria Report, it was observed that 219 million malaria cases as well as 435,000 fatalities were registered. In 2017, 17 countries in the WHO African Region accounted for over 80% of global malaria-related deaths [6]. Increasing severe cases of malaria in the world lead to consider malaria as a global priority under resolution WHA42.30 (1989) and the WHO was alerted to make every effort to move appropriate scientific financial and human resources to alleviate this misery [7]. The life cycle of *Plasmodium* is complicated and consists of two phases: sexual and asexual. The sexual phase of the parasite's life cycle occurs in the vector mosquitoes and the asexual phase occurs in humans (intermediate host) [8]. Infected female mosquitoes of the genus *Anopheles* only transmit malaria to humans. [9]. Malaria is one of the top ten causes of mortality mainly in Sub-Saharan Africa [3].

1.2 Dengue

Dengue virus of the Flaviviridae family causes dengue fever and it is spread widely in tropical and subtropical areas. Dengue control strategies have been challenging, since no vaccine or particular medication are available. As per WHO report, dengue fever has been identified in over 100 countries with an estimated 50–100 million cases each year and 2.5 billion people at risk. There are 500 000 DHF patients with a 5% case fatality rate (20,000 deaths). According to a recent report, dengue infections are 390 million and episodes of dengue fever 96 million per year throughout the world, WHO predicted three times less dengue burden than this [10]. *Aedes aegypti* resurgence, as it is the primary vector in many locations and the rapid global spread of a secondary vector, *Aedes albopictus*, and the epidemiologic picture of dengue fever has worsened [11]. *Aedes* female mosquitoes consume blood and lay around 100 eggs within just 3 days. Ovarian development is triggered by stomach distension. When their consumption of blood is very less for egg generation effectively, and since smaller blood meals create fewer eggs, refeeding along with repeated bites by similar females happens [12]. Dengue infection can be asymptomatic or symptomatic, with symptomatic infections accounting for roughly 20% of all cases. In general, dengue fever manifests after 3 to 10 days of an infected mosquito bite. Dengue infection can start off as a mild "flu-like" sickness with symptoms that are similar to malaria, chikungunya, Zika, and influenza. Retro-orbital pain, fever, acute headache, intense joint and muscular pain, and nausea are all symptoms of the condition. Dengue can cause more serious disease symptoms, such as hemorrhage and subsequent vascular leaks, in addition to self-febrile diseases. Patients may experience pleural effusion, hemorrhage, thrombocytopenia (<100,000 platelets/mL), an increase in hematocrit levels, abdominal pain, vomiting, restlessness, and a sudden drop in temperature when the condition is severe [13]. The trend shows that the disease has been continuously transmitted starting from the 1950s, exacerbated with the help of urbanization, globalization, and also due to failed control of vectors, resulting mainly in increasing virus infection as well as virus transmission in many places [3].

1.3 Chikungunya

An alphavirus which belongs to the Togaviridae family is the major cause of chikungunya which means "disease that bends up the joints" in the Tanzanian Makonde dialect [14]. It is a mosquito-borne arboviral disease spread by mosquitoes of the *Aedes* species, particularly *Aedes aegypti* and *Aedes albopictus*. Previously it was prevalent in tropical countries such as Africa, Southeast Asia, and the Indian subcontinent, the disease has seen a significant regional extension in recent years. In 2005-06, an outbreak in India resulted in approximately 1.4 million recorded cases, while another significant outbreak in La Réunion resulted in over 250,000 confirmed cases [15]. The majority of CHIKV patients experience acute symptoms 2 to 6 days following the infective insect bite. In 2005–2006, the frequency of asymptomatic infections on Reunion Island was estimated to be between 5% and 10%. The first symptoms appear suddenly and linger for roughly a week before subsiding on their own. The acute stage is sustained for 10 days following the commencement of the disease. High temperature, headache, arthralgia, and back discomfort are major symptoms. In adults, this disease is linked to extreme tiredness, anorexia, myalgia, and vomiting along with transitory confusion in old people [16]. For CHIKV, there are two separate transmission cycles: one is an enzootic sylvatic cycle and the other one is an endemic urban cycle. During small outbreaks in Africa, the enzootic transmission cycle can spread to adjacent humans, also enzootic mosquito vectors are most probably engaged for inter-human transmission. Many arboreal *Aedes* mosquito species (*Aedes vittatus, Aedes luteocephalus, Aedes vigilax, Aedes furcifer, Aedes camptorhynchites, etc.*) are likely vectors in the African sylvatic cycle, with nonhuman primates serving as a reservoir or amplifying hosts [17].

1.4 Japanese encephalitis

Japanese encephalitis mostly occurs in Asia. The virus that causes Japanese encephalitis is the (JEV) Japanese encephalitis virus which belongs to Flavivirus genus and family Flaviviridae. This Flaviviridae family includes viruses that cause West Nile, Zika viruses, and dengue. JEV causes severe neurological manifestations, despite the fact that many flaviviruses can cause encephalitis. Because of the frequent neurological sequelae, the virus causes more disability than any other arthropod-borne virus. JE virus is RNA virus (single-stranded) having characteristics similar to those of other flaviviruses. JEV is spread by mosquitoes of the genus *Culex* and is found in Asia's wild-wading birds [18]. Japanese encephalitis mostly affects children in endemic areas [19]. *Culex tritaeniorhynchus, Culex vishnui,* and *Culex gelidus* are the most common JEV vector species. The pathogen is transmitted to the vector during a blood meal on an infected host, causing a systemic infection that leads to an infection of the salivary glands, allowing the virus to be transmitted to another host via blood feeding. The virus must overcome several physiological barriers to establish a systemic infection, particularly in the mosquito's midgut and salivary glands [20]. Although there are JE vaccines that are safe as well as effective, JE remains a health concern for the public belonging to countries that are endemic and living with limited resources. As a result, case-based surveillance must be implemented in most countries having fast transmission rates [3].

1.5 Rift valley fever (RVF)

RVF also comes under mosquito-causing viral disease discovered in Kenya in 1931. Human diseases and deaths, as well as high livestock abortions and deaths, have all resulted from RVF outbreaks. RVF virus is a Phlebovirus that belongs to the Bunyaviridae virus family [21]. RVFV has been obtained from over 53 species belonging to eight genera of the Culicidae family. Apart from *Culex* high number of *Aedes* mosquitoes also spread this virus. Eggs of *Aedes* latent inside the soil are usually induced to hatch within the first 1–2 days after flooding, resulting in the emergence of a minimum of one extremely large generation of *Aedes* mosquitoes that are infected. The RVFV is subsequently transmitted by mosquitoes to amplifying vertebrate hosts, which can start the epizootic cycle. Species from livestock, particularly populations of sheep, experience severe death, and around 100 percent of abortion after being infected by primary *Aedes* vectors, high viremias are enough for infecting the numerous secondary mosquito vector species. RVF monitoring, specific ground monitoring, animal immunization and vector control are the specific control measures [22].

1.6 West Nile Fever

West Nile virus also belongs to genus *Flavivirus*, family Flaviviridae. Alfuy, Stratford, St. Louis encephalitis, and Usutu also belong to the same family and they are also transmitted by mosquitoes which can cause severe, frequently fatal diseases in humans. The most prevalent vector present in Africa and also in the Middle East is *Culex univittatus* whereas *Culex. poicilipes, Culex. decens, Mimomyia spp, Aedes albocephalus,* and *Culex. neavei* also play a role in some locations. The most prevalent vectors in Europe are *Culex pipiens, Culex modestus*, as well as *Coquillettidia richiardii*, whereas the most common in Asia are *Culex quinquefasciatus, Culex tritaeniorhynchus,* and *Culex vishnui*. The virus can be transmitted transovarially in *Culex tritaeniorhynchus, Aedes aegypti,* and *Aedes albopictus,* however at low rates [23]. Fever, malaise, headache, myalgia, nausea, vomiting, and rash are among the symptoms of West Nile fever, which lasts 3 to 6 days. Hundreds of people were affected in certain epidemics in Romania, Russia, and Israel, with high neurologic diseases and mortality [24].

1.7 Yellow fever

Flavivirus from the family *Flaviviridae* is the virus responsible for causing yellow fever. The virus is having a restricted host range, and it survives in nature due to transmission between nonhuman primates and mosquitoes. The vectors are mostly *Aedes* (*Stegomyia*) genera in Africa and *Haemagogus* in South America. When sylvatic mosquitoes attack humans after feeding on the viraemic monkey, they can act as a viraemic host, especially for transmission between humans, which is mostly caused by *Aedes* species. Yellow fever posed a substantial risk to human health from the 18th to the early twentieth century, with epidemics occurring in coastal towns as well as cities distant from endemic areas present in Europe, North America, and the Caribbean [25]. Yellow fever vaccinations are presently available against flaviviral diseases in humans [3].

1.8 Zika fever

The Zika virus (ZIKV) is a flavivirus that is spread by mosquitoes and belongs to the Flaviviridae family. ZIKV is part of the Spondweni serocomplex and is thought to have originated in Sub-Saharan Africa's forest regions, where it is thought to have survived through enzootic sylvatic cycles among mosquitoes as well as non-human primates. Monkeys have been known to suffer cyclic epizootics on a regular basis [26]. Infected mosquitoes of the *Aedes* genus, especially *Aedes aegypti* in tropical areas, transmit ZIKV. ZIKV has the potential of sexual and vertical perinatal transmission. There have already been two cases including sexual transfer and two cases having vertical perinatal transmission documented [27,28,29]. Congenital, perinatal, and sexual transmission are all non-vector routes of Zika virus transmission. Blood transfusion, animal biting, and laboratory exposure have all been mentioned as possible modes of transmission. ZIKV infection clinically is not so specific mild fever or rash etc. makes it more confusing with other diseases mainly dengue and chikungunya. Public health experts should be concerned about ZIKV's adaptation to an urban cycle including *Aedes* *aegypti* as well as other mosquitoes of the *Stegomyia* subgenus, which act as vectors and humans acting as amplification hosts [29].

As we can see, mosquitoes are the major vector, causing transmission of most of the above mentioned diseases. Mosquitoes are a significant category of insects when it comes to disease transmission and public health particularly. Mosquito populations are increasing dramatically, thereby becoming a severe challenge for vector control in many countries. Mosquitoes are found in tropical as well as subtropical regions and there are around 3500 species. Chikungunya and also dengue fever is mostly spread by *Aedes aegypti* mosquitoes, which acts as a vector and infects 2.5 million people each year [30].

2 Mosquito control methods

A complete and thorough approach to pest management is used to prevent and control mosquito-borne diseases around the world. Efforts are not aimed at completely eradicating mosquito populations, but rather at reducing mosquito populations in order to lower the risk of disease transmission. Mosquito management methods include eliminating nesting areas and controlling mosquito larvae and adults. The best technique for killing mosquito larvae and pupae in the water is to use larvicides, which are chemical pesticides applied to breeding locations. Monomolecular surface films, methoprene, larvicidal oils, neurotoxic insecticides, chemical insecticides, larvicidal microorganisms and plant-derived compounds are examples of larvicides that are available in powder, tablet, or liquid form. When it comes to mosquito control, adulticides are usually less effective. Adulticides originating from microbes, plants, minerals, organophosphates, synthetic compounds, and some natural pyrethrins are a some of the adulticides used to control mosquitoes [31]. Environmental modifications are referred to the temporary changing of the water bodies where larvae develop, actions that reduce vector mosquito larval breeding places. These strategies may be appropriate when permanent elimination of aquatic habitat by environmental alteration is not possible, or when the intermittent presence of water is required for other activities, as in agriculture field [32].

2.1 Physical methods

Once a week, the water in fountains, swimming pools, and rain barrels must be changed. It is necessary to wear full-sleeved garments at dawn and dusk and to close doors and windows with screens to protect from mosquitoes [33].

2.1.1 Mosquito nets

Mosquito nets are found to be more protective than coils or repellents. These nets do not cause any health-related problems. Medicated nets and non-medicated nets are two different types of nets [34]. Medicated nets are those which are usually made by using tablets of K-O, along with 25% of deltamethrin. In this one tablet is mixed in one litre of water, the net has to be soaked inside for a minimum of ten minutes, and afterward, it has to be dried in a refrigerated place. This mosquito net is effective against mosquitoes for six months. The medicated nets have been approved by the World Health Organization, and they are more effective than coils [35].

Non-medicated mosquito nets can be composed of different type of materials including polyester and cotton. To protect yourself from mosquito bites, the type of net you use is important. It is essential to purchase a mosquito net with a mesh size large enough to allow air and small enough to stop mosquito entry [36].

2.1.2 Mosquito traps

Female mosquitoes are lured and captured using mosquito traps. These traps imitate mosquito attractants including body heat and carbon dioxide exhaled. Because the majority of the traps are driven by propane as well as electricity, they are completely safe to use. When a mosquito is drawn to a trap, usually it will attach to the trap's sticky surface and be electrocuted [37].

2.2 Mechanical methods

Devices such as mosquito magnets and electrical mosquito zappers are used in the mechanical method.

2.2.1 Electric Mosquito zapper

This gadget uses UV light to catch mosquitoes, which are subsequently killed when they come into contact with the fatal amount of electric charge.

2.2.2 *Mosquito magnet*

Its concept is focused on imitating mammalian characteristics such as the release of heat, carbon dioxide, also moisture. Mosquitoes are drawn in and die if they come too near to the gadget. This octenol-based magnet may be used to repel sand flies, midges, black flies, and mosquitoes [38].

2.3 Chemical methods

According to integrated pest management (IPM) plan, pesticides for mosquito control have been proved to be very effective and safe; nevertheless, only a few chemicals are currently licensed for mosquito control [39]. For many years, chemical pesticides have been used to control the mosquitoes. Chemical insecticides have made an important contribution to agriculture by reducing hazardous pests and insects that can reduce a crop's net output. Organophosphates, pyrethroids, carbamates, and organochlorines are the principal insecticide classes that are used mostly. These pesticides are used to suppress a variety of mosquito species that are implicated in the spread of diseases like Dengue Fever, Malaria, Japanese encephalitis, and Lymphatic filariasis [40]. Demerits of using chemical pesticides like being more expensive, developing resistance in mosquitoes, requiring more effort etc., and these pesticides can kill certain important species of mosquitoes.

2.3.1 *Synthetic repellents*

DEET, the most effective synthetic repellent, is toxic and it has the ability to emit carbon monoxide and also natural odours comparable to those generated by the human body. IR3535 (3- [N-Butyl-N-aminopropionic acid) is a better insect repellent than DEET since it lasts longer and is more efficient. Plant-based repellents are also effective. Essential oils have a limited duration of effect and are easily vaporized [41].

Some examples are:

- Permethrin
- Icaridin
- DEET (N,N-diethyl-m-toluamide)
- Bog Myrtle [30]

DEET (N, N-diethyl-3-methyl toluamide) is the finest mosquito repellent which is widely used synthetic type even though it shows negative side effects. The application of DEET is thought to have a maximum biting inhibition rate of 88.7- 92.5 percent [42]. However, the study found that DEET can cause muscular twisting, seizures, slurred speech, nausea, and rashes, as well as affect motor capacity, sensory disruption, cognitive capacities, and memory degradation. However, DEET does not have long term effect on *Anopheles* which cause malaria. DEET can cause harmful effects for youngsters, nursing women, or pregnant people.

Icaridin is the common name for hydroxyethyl Isobutyl piperidine hydroxyethylcarboxylate. It has no colour or odour and it is used to kill insects [43]. It operates similarly to DEET in that it is used to block or shade insects' olfactory receptors, making it difficult for mosquitoes to detect people. It has been recommended over DEET because it is effective in lower concentration compared to DEET [44]. Permethrin is another safe chemical pesticide to use on camping equipment, nets, shoes, and clothing, but not on humans. It is used for killing ticks and mosquitoes. Permethrin-treated clothes are harmless for people; however, these items should not be applied to the skin. It should be applied on the textile as a spray. It has six-hour duration of action. Permethrin is derived from the naturally occurring pesticide pyrethrum. When combined with DEET, it provides increased protection [30].

2.3.2 *Larvicides*

Larvicides such as petroleum oils and Paris green (copper aceto arsenite) have been successfully employed. Despite their low cost and outstanding efficiency, the Paris green usage is no longer suggested due to the arsenic metal toxicity in the formulation. The main vector management technique in India is larviciding the breeding sites using organophosphate insecticides such as temephos and fenthion; however, fenthion has recently been removed from usage in India due to pesticide resistance development. Temephos, for an instance, has low mammalian toxicity. Synthetic pyrethroids are also showing effective results, but they have been shown to be highly harmful to aquatic non-target organisms particularly and therefore they are not utilized for larval control [45].

2.3.3 *Indoor residual Spray*

To kill mosquitoes, stable pesticide formulations are applied to the inside sprayable surfaces of houses. This reduces the life span of female mosquitoes, lowering insect density and thereby reducing malaria transmission.

2.3.4 *Space spray*

The practice of applying a pesticide after heating chemical in liquid form to generate thin droplets which look like smoke as well as fog is known as space spraying or fogging. It is mainly used in emergency settings to stop epidemics and quickly reduce adult mosquito populations, leading to a reduction in transmission.

2.3.5 *Long lasting Insecticidal Nets (LLINs)*

The operational success of an insecticidal treating nets programme is limited because there is loss of Insecticidal efficacy of treated nets after washing the nets and related very less retreatment rates. LLINs limit human and mosquito interaction, resulting in lowering of sporozoite as well as parasite rates. The activity of polyester nets stays 3–4 years, while polyethylene nets last 4–5 years. Five brands that got recommendations from World Health Organization under Pesticide Evaluation Scheme, is net of Olyset® which only received complete approval, whereas Perma-Net-2.0®, Net Protect-®, Duranet-®, and Interceptor-®, as well as K-OTab1- 2-3® and ICON-MAXX®, have received interim approval [45]

2.4 Biological control methods

There is no evidence of pollution or resistance to biological agents in the environment. Their impacts on living things, such as humans, domestic animals, and wildlife, are less. The value of biologically managing the mosquito vector is also reflected in the biological control agent's functional diversity. Furthermore, with so many present as well as future strategies, are focused on genetically modified microbes use to stop the parasite from developing within the mosquito vector or maybe it targets the vector itself. Biological control of mosquito vectors is seen as a vital component of the recently launched malaria eradication program [46].

2.4.1 *Entomopathogenic Fungi*

Entomopatghogenic fungi can be kept under major biological control strategies which can be augmentation, conservation or classical biological control. *Entomophaega maimaiga, Z. Radicans* are two major examples of classical biological control [47]. *Entomophaga maimaiga*, a particular disease of the gypsy moth *Lymantria dispar*, only infects one or a few closely related species. *Beauveria bassiana*, on the other hand, infects a wide spectrum of arthropods in a wide range of settings like fields, forests, and also greenhouses. Most parasitoids and predators are compatible with entomopathogenic fungi in general [48]. *Zoopthera radicans* causes epizootics in spotted alpha alpha aphids. *Hypho mycete* fungi are inundative biocontrol agents as they are easy to formulate and mass produce.

Bacterial agents

Entomopathogenic bacteria, one of which is *Bacillus thuringiensis* (*Bt*), is known from 1900s, but for control of dipterans considering it only started from 1977 after *B. thuringiensis* serovar *israelensis* (*Bti*) discovery and *Bacillus sphaericus (Bsp)* strain 1593 which was highly toxic. Various screening programmes have been started after this discovery with the goal of isolating a number of novel mosquitocidal strains. This led to the discovery of a large range of Gram-positive bacteria, which also includes *Bt* and *Bs* isolates as well as different other bacteria. Some of them like *Brevibacillus laterosporus* and *Clostridium bifermentans* are insecticidal agents but are not used commercially. The level of mosquitocidal activity and specificity of each strain isolated has been determined. The elements responsible for the insecticidal action of most of these bacteria have been discovered and characterized, and the presence of protein inclusion bodies generated during sporulation is the primary cause of toxicity. These poisonous components are known as Cry and Cyt toxins in the case of *Bti*, and Bin toxins in the case of *Bs*. [49].

- *Bacillus thuringiensis* var *israelensis* or *Bti*

It is a spore-forming entomopathogenic bacterium and it was initially identified in Israel in 1976. It is presently the most potential biocontrol agent against mosquitoes (especially *Culicidae* and *Simulidae*) as well as black flies, and it may be used alone or also as a part of a comprehensive strategy for control of vectors. *Bti* is gram-positive bacteria that can grow in vitro in chains up to 3-3.5μm long. At the time of spore growth, protein inclusion crystal called as a parasporal body develops in the cell. It is made of several proteins having various sizes from 27 kDa to 138 kDa, known as the delta-endotoxins. These proteins are mosquitocidal. Complete spore crystal complex possesses high toxicity because of synergistic interaction among 25 kDa protein (which is the proteolytic product of the 27 kDa protein) and also one or sometimes more additional proteins. At the time when larvae of sensitive animals eat *Bti* spore-crystals having toxic proteins (pro toxins), these proteins are solubilized inside the alkaline pH present in the larval gut and get activated as toxins. These toxins primarily attack the plasma membrane situated in the midgut epithelium. When toxin of *Bti* binds to certain receptors present inside the plasma membrane, it makes lipids in detergent-like rearrangement, causing membrane rupture and cytolysis thereby killing the larvae.

- *Bacillus sphaericus*

Other spore-forming aerobic bacteria, such as *B. sphaericus*, are also highly insecticidal against mosquito larvae. In 1965, USA yielded the first insecticidal strain of *B. sphaericus*. Based on the H-antigen, *B. sphaericus* strains are classified into several serotypes. Serotype H5a and 5b are the most insecticidal strains. *B. sphaericus* develops in culture as 2–3 µm long rods that generate spherical spores at the rod's end during sporulation. This crystal is absent in less insecticidal strains. The most essential parts of the crystal include 2 proteins of size 51 kDa and also 42 kDa that function like binary poisons since both of the proteins are necessary for causing toxicity. When the crystal is dissolved in alkali, its toxicity is lessened. *B. sphaericus*, like *Bti*, operates through the larvae's gut. The inclusions get solubilized in the larval midgut because of alkaline pH once the crystal-spore cell is swallowed by sensitive mosquito larvae. Protoxin proteins with sizes of 51 and 42 kDa are transformed (activated) into proteins with sizes of 43 kDa, and 39 kDa, respectively. Protein toxins bind to the cells in stomach caecum as well as posterior mid-gut. Intoxication symptoms appear within 30-60 minutes. Unlike *Bti*, there is no evidence of widespread destruction of mid-gut cells in *B. sphaericus*. The toxin's selectivity is influenced by variances in the number of target sites to which it binds. *Culex pipiens* which is a susceptible species, toxin protein binds to stomach caecum or else mid gut whereas in *Aedes aegypti* which is resistant species it does not bind [50].

- *Clostridium bifermentans*

The first anaerobic isolate with strong mosquitocidal activity, CH18, was described in 1990 as a result of screening procedures aiming at identifying new strains of insecticidal bacteria. This isolate has been found in mangrove swamp soil in Malaysia and it was later on identified as *C. bifermentans* serovar *malaysia*. *C. bifermentans* serovar. *paraiba* (*Cbp*), a new mosquitocidal *C. bifermentans* strain isolated from a secondary forest floor in 1997, was recently reported. Both *C. bifermentans* strains as well as *Bti* strains have moreover similar insecticidal spectrum although their toxic factors are not the same; therefore, they are more similar to *B. thuringiensis* strains claa-2 B. These two strains have a highest toxicity to *Anopheles* larvae, which is followed by *Aedes* and *Culex* in case of toxicity. *Clostridium* is a large bacterial genus that includes several human harmful strains. As a result, more precise investigations were undertaken to determine how safe the *Cbm* strain is in terms of potential bioinsecticide. All non-target invertebrates and vertebrates investigations verified the toxicity of these strains. Parasporal bodies and any other morphological trait linked with toxicity are not produced by *Cbm* isolate. Amorphous structures near the spores have been seen, and it has been postulated that these may be responsible for toxicity [49].

- *Brevibacillus laterosporus*

Brevibacillus laterosporus, is also a spore-forming bacteria which produces canoe-shaped lamellar bodies near the spore. Mosquito strains, 16-92 (isolate 921) as well as LAT006 (isolate 615) are most toxic strains which are recently been found [51]. The toxicity of two strains is high towards the *Aedes aegypti* and *Anopheles stephensi* species, compared to them it shows less effect against *C. pipiens*. Both strains are capable of forming crystalline inclusions which are of different shapes and sizes and are harmful [52]. 615 crystals purified from *B. laterosporus* are as toxic to *Aedes aegypti* and *Anophele stephensi* as *Bti.* The crystal components nature which are causing toxicity is yet to be identified.

Larvivorous fish

Using predatory fish which feed on mosquito larvae was one of the old recommended ways of controlling vector illnesses. Before the 1970s, mosquito management was dominated by the freshwater *Gambusia affinis*. This species was widely imported from around the world for controlling mosquito vectors. Fish species of Cyprinodontidae family also have been utilised extensively for larval control. Larvivorous fish are considered to be more effective than chemical agents. The anopheline larval density was dramatically decreased when *A. sinensis* was challenged with a mixed population including *Cyprinus carpio, Tilapia* spp, and *Ctenopharyngodon idella*. When numerous *Anopheles* species are exposed to a mixed-up population having *Catla catla, Ctenopharyngodon idella, Cyprinus carpio, Labeo rohita,* and also *Cirrhinus mrigala*, the larval density dropped by 81 percent. The potential influence of *Poecilia reticulate* in anopheline management was demonstrated in different varieties of riverbed pools present under so many large dams situated in Sri Lanka [46].

2.5 Resistance Phenomena

Resistance to insecticide is defined as the ability of an insect population of being capable of tolerating insecticide doses that in general would kill most of individuals present in a normal population belonging to the same species. As a result of the increased worldwide circulation of plant materials, it is known that mosquitoes can travel to different parts of the world, which helps them to spread resistance genes to the plagues they have, that is why resistance development shown by mosquito disease vectors mainly is of international importance. Majority of mosquito vector control methods for human diseases rely on outdoor spraying, impregnated nets, or inside residual spraying with chemical insecticides. Almost 84 mosquito species have evolved resistance to each of the main pesticide classes.

Mosquito vectors can develop pesticide resistance through two mechanisms: By altering the target site of action as well as metabolic resistance, which is commonly referred to as an accelerated rate of pesticide detoxification. Resistance to behavior and resistance to reduced entry from the cuticle as well as cross barrier are two less prominent mechanisms that create resistance in insects [53]. Because of putative several-site interactions among the viruses and also their targets, it was anticipated that insect resistance to *Bacillus sphaericus* and *Bacillus thuringiensis* serovar *israelensis* would not arise. Due to the obvious existence of four separate toxins with putatively different mechanisms of action, no reports were identified regarding field resistance to *Bacillus thuringiensis* serovar *israelensis*. The BinB component due to its single receptor interaction with Bin toxin it must be considered only one molecule for *Bacillus sphaericus* in *C. pipiens*. During the previous four years, resistance to *Bacillus sphaericus* has been reported in Brazil around 10-fold and in India150 fold and France upon *C. pipiens* around 10,000-fold. Recently, two further reports from China around 25,000-fold and in Tunisia 2,000-fold revealed that *Bsp* resistance can emerge in the field when the bacteria are employed extensively. Different *Bsp* strains including recombinant *Bacillus sphaericus* expressing other toxins from those other mosquitocidal bacteria must be taken into account. However, putting the *Bacillus sphaericus* crystal toxin genes only into natural mosquitoes diet (e.g. Cyanobacteria) poses a risk since the larvae would be subjected to continual selection pressure. Apart from that, a better understanding of the mode of action, as well as the identification of receptors for other mosquito species and the *Bacillus sphaericus* crystal toxin intracellular activity may provide useful tools for identifying other resistance mechanisms for predicting and reducing resistance [49].

3 Conclusion

Mosquito borne diseases are severe and increasing day by day. It can cause mild disease to severe manifestation like death in human beings. These diseases are causing epidemics in various places as well as few are spreading globally also. Proper treatment and vaccination are still not found for several mosquito borne diseases. Therefore, search for long lasting and effective mosquito control methods are important. Using bacteria as biological control is more effective and also it overcomes various demerits of chemical control methods. Mosquitoes can easily acquire resistance against most chemical pesticides but in case of biological control it is rare. Biological management is long-lasting, affordable, and safe for living species and the environment; it does not destroy the pathogen, but rather restores them to natural balance. Microbial insecticides are currently the most important component of the bio-pesticide sector. *Bacillus thuringiensis* and *Bacillus sphericus* biopesticides tends to remain longer in the environment, particularly in dirty water, and hence may be a viable choice for long-term mosquito control. The majority of pesticidal microorganisms have been isolated from the terrestrial environment. The use of these microbial insecticides instead of synthetic pesticides in mosquito control might be cost-effective and reduce pollution.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare no conflicts of interest.

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