Vector-Borne Diseases & Treatment

Chapter 4

Mosquito Borne Diseases: Current Status and Control Approach in India

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1. Introduction

Hematophagous arthropods pose a serious threat to human health because of their ability to transmit hundreds of disease carrying viruses, bacteria, protozoa and helminthes to vertebrate hosts, particularly humans [1]. Diseases transmitted to humans by an arthropod or another living organism (vector), is known as vector borne disease that accounts for 17% of the estimated global burden of all infectious diseases [2]. Annually, more than 1 billion vector borne infections take place and more than 1 billion people die from such diseases [3]. Historically vector borne diseases were responsible for more human deaths than all other causes combined [4]. Some of the greatest plagues that mankind has observed such as the 'Black Death' in Europe (14^{th} Century) and the epidemics of yellow fever were caused due to such diseases [5]. First discovered in 1877 by Sir Patrick Manson who demonstrated that *Wuchereria bancrofti* (a parasite of humans causing filariasis), was transmitted by a mosquito, *Culex pipiens fatigans*, since then many medically important disease pathogens have been found to be transmitted by blood sucking arthropod vectors [5].

Vector-borne diseases stand as a major public health problem, mainly in countries belonging to tropical or sub-tropical region, where proper sanitation, consumption of safe drinking water resources and regular surveillance is a huge challenge [2]. However, owing to the impact of globalisation and increased human mobility throughout the world due to air travel, these diseases no more remain problem of the tropics only rather they pose a major threat to the whole world [5]. Some of these diseases, if left untreated prove to be fatal, whereas some other leave patients disfigured or disabled [2].

Of all disease-transmitting insects, mosquito which has a slender body and long needle shaped mouth parts specialised for sucking blood from vertebrates, is the greatest menace. Mosquitoes are the vectors of several dreadful diseases which include tropical diseases like Malaria, filaria and viral diseases like dengue, Japanese encephalitis, yellow fever, west nile fever, zika, chikungunya *etc* which together are responsible for several million deaths and hundreds of millions of cases every year [6]. There exist about 3000 species of mosquito of which around 100 are vector of medical significance [7]. Most of the mosquito borne viral infections cause typical manifestations like haemorrhagic disease, encephalitis, biphasic fever, flaccid paralysis and jaundice [8].

Many control strategies have been designed and followed since centuries ago but despite of such efforts and programmes, mosquito borne diseases are prospering throughout the world [9]. Earlier mosquito fauna were limited to the low land areas only but as a result of immense climate change, their geographical distribution has expanded to higher altitudes and latitudes [10]. Due to failing efficacy of vector control programmes, there has been a dramatic emergence and resurgence of mosquito borne diseases [11].

India owing to its subtropical and tropical climatic parameters (high rainfall and relative humidity), lack of proper drainage system, water stagnation and vast vegetation cover provides the favourable ambience for mosquito growth and proliferation [12] and thus to the transmitted diseases. India is endemic to five of the mosquito borne diseases namely, Malaria, dengue, chikungunya, filaria and Japanese encephalitis. Moreover three confirmed cases of Zika has also been reported from India very recently [13]. This chapter focuses on the above mentioned mosquito borne diseases and the burden it has imposed on India.

2. Major Mosquito Vectors

In India, there are mainly four mosquito genera carrying disease causing pathogens namely, *Anopheles*, *Aedes*, *Culex* and *Mansonia* each causing different diseases.

Mosquitoes belonging to the genus *Anopheles* are responsible for transmission of malaria. About 380 species of *Anopheles* occur around the world of which 60 species are act as vectors of malaria to humans [7]. In India, 58 anopheline mosquitoes exist, of which only six taxa act as malaria vectors namely, *An. culicifacies, An. fluviatilis , An. minimus, An. dirus, An. sundaicus and An. stephensi* [14]. *Anopheles culicifacies* also known as the rural malaria vector in the country and *An. fluviatilis*, found in the plains and foothills accounts for 60-70% and 15% of the annual malaria infections respectively [15]. Moreover, *An. minimus* breeding in streams of northeastern foothills, *An. dirus* found in forest areas of northeastern states of India, *An. sundaicus* found in brackish waters (their breeding sites) in Andaman - Nicobar islands and *An. stephensi* (known as the vector species of urban malaria) also contributes towards the total annual malaria infections [15]. Control of malaria in India is basically concerned with the

control of *An. culicifacies* [15].

Mosquitoes belonging to the genus *Aedes* house a number of pathogenic arboviruses causing dengue, dengue haemorrhagic fever, chikungunya, zika, yellow fever, west nile fever *etc*. They have also been shown to transmit filariasis [7]. Around the world there are approximately 950 species of *Aedes* of which two species *Aedes aegypti* and *Aedes albopictus* pose the greatest public health concern [7]. *Ae. aegypti* has its origin in Africa whereas *Ae. albopictus* originated in Asia and has now expanded its geographical distribution through different countries of world as a result of human activities [16]. *Ae. albopictus* has its distribution northern than its counterpart *Ae. aegypti*, owing to its ability to survive through the colder seasons by entering into dormancy [16]. Earlier *Ae. aegypti* was called as the primary vector of dengue virus (DENV), whereas *Ae. albopictus* was known as the secondary vector, however recent studies have shown that both the species contribute equally towards DENV infections. Both the species are distributed throughout Indian subcontinent and their breeding habitat mainly consist of artificial containers or water logged vessels such as bamboo stumps, tyres, cemented tanks *etc* [12]. The *Ae. aegypti* mosquito vector was found to be prevalent in the western, northern, Indo Gangetic and eastern plains, Assam valley and the coastal areas of Orissa state in India. The elevation, type of relief, terrain, density of population, water storage practices in drought-prone regions and high rainfall had direct relationship with the prevalence of the species [17]. Altitudes above 1000 metres have been reported to be unfavourable for the *Ae. aegypti*. *Ae. albopictus* has been reported to be encountered in the peripheral areas of Indian towns where it has replaced the *Ae. aegypti* populations [17].

Another disease carrying mosquito genus is *Culex*, which consists of around 550 species [1]. Most of the *Culex* species inhabits tropical and subtropical countries. Species such as *Culex quinquefasciatus* is a vector of bancroftian filariasis where as others such as *C. vishnui and C. tritaenorhynchus Cx. Pseudovishnui, C. gelides and C. fuscocephala* transmits disease Japanese encephalitis (JE) [18]. Other species transmit arboviral diseases such as St Louis encephalitis virus and West Nile virus [19]. In India, main concern to *Culex* mosquitoes are due to bancroftian filariasis and Japanese encephalitis.

The genus *Mansonia* comprises of mosquitoes mostly found in marshy areas in tropical countries, some of which act as vectors of brugian filariasis. This disease is common in south India, Indonesia and Malaysia. In 1980, the virus for JE was isolated from *M. annulifera*, indicating its potency in transmission of JE also [20].

3. Major Mosquito Borne Diseases in India

Mosquitoes act as vector for numerous human diseases worldwide (**Table 1**). However in India they transmit 5 endemic diseases which are explained below. Also has been explained Zika, a disease that may have a serious outbreak in the upcoming season.

Table 1: Mosquito vectors and the disease transmitted by them worldwide

Mosquito vector	Disease	Continents at risk
Anopheles	Malaria	South America, Africa, Asia
Aedes	Dengue	South America, Africa, Asia, North America
	Chikungunya	North America, South America, Europe, Africa, Asia
	Yellow fever	South America, Africa
	Zika	Africa, Asia, South America
	La Crosse encephalitis	North America
Culex	Japanese encephalitis	Asia, Australia
	St. Louis encephalitis	North America
	West Nile fever	North America, Europe, Africa, Asia, Australia
Anopheles, Culex, Mansonia, Aedes	Lymphatic filariasis	South America, Africa, Asia, Australia
Aedes, Coquillettidia, Culex	Eastern equine encephalitis	North America, South America
Culex, Culiseta	Western equine encephalitis	North America, South America

3.1. Malaria

Among mosquito borne diseases, malaria poses one of the greatest threat to human health. Malaria is an illness caused by parasites of *Plasmodium* species transmitted exclusively by the bites of *Anopheles* mosquito. Malaria is endemic in 91 countries, putting approximately 40% of the world's total population at risk. Globally around 500 million cases of malaria infection occur causing up to 2.7 million deaths annually [6]. Southeast Asian region stands 2nd just after sub Saharan African region in total malaria cases throughout the world [2]. India contributes to 80% of the malaria cases occurring in Southeast Asia with around 24 million cases per year, this endemicity is attributable to the presence of multiple vector species and India's diverse ecology [3,21].

In 2016, around 1,090,724 malaria infections were reported in India, causing 331 deaths [22]. Malaria is endemic in most of the parts of India excluding elevations above 1800 metre and a few coastal areas [23]. About 90% of the Indian population reside in malaria endemic areas [24]. The Indian National Malaria Eradication Programme (NMEP) has reported that 2.5 to 3 million malaria cases causing 1,000 malaria deaths occur annually in India. The dominant causative agent in India is *Plasmodium vivax* (60-65%), whereas malignant malarial protozoa *i.e. P. falciparum* accounts for 30-35% of the infections [25]. Malaria was nearly eradicated from India in the early 1960s but the disease has re-emerged as a major public health problem [26]. Currently, the Eastern and Central states, *i.e.* Orissa, Jharkhand, West Bengal, North Eastern India, Chhattisgarh, Madhya Pradesh contribute to the bulk of malarial infections (>65%)[27,28]. Moreover, majority of the death attributable to malaria are from Orissa and other forested areas occupied by ethnic tribes in the country. The availability of diverse malar-

ia parasites and vector species, variable microenvironment favouring growth and proliferation of both the parasite and vector along with a highly susceptible human population have resulted in higher malarial infection rates in tribal areas [29].

The malaria incidence and deaths due to malaria have reduced significantly in recent years. During the period 2000 to 2015, malaria cases declined by 44% from 2.03 million to 1.13 million and deaths declined by 69% from 932 to 287. The Pf percentage remained around 50% from 2000 to 2013, but rose to 65.6% in 2014 and 67.1% in 2015 [30]. Encouraged by the success achieved in malaria control in recent years, the National Framework for malaria elimination in India 2016-2030 was launched in February 2016 with a goal to eliminate malaria throughout the country by 2030 and maintain malaria free status wherever malaria transmission has been disrupted. The strategies for achieving the above goals [30] have been pointed out as:

- Early diagnosis and radical treatment
- Case-based surveillance and rapid response
- Integrated vector management (IVM)
- Indoor residual spray (IRS)
- Long-lasting insecticidal nets (LLINs) / Insecticide treated bed nets (ITNs)
- Larval source management (LSM)
- Epidemic preparedness and early response
- Monitoring and evaluation
- Advocacy, coordination and partnerships
- Behaviour change communication and community mobilization
- Programme planning and managements

Though there is no vaccine available for malaria in India, chloroquine is the first line treatment for vivax malaria. For *P. falciparum* infection, chloroquine is only administered inin low risk and chloroquine sensitive areas [31]. It has been reported that chloroquine has been found to result in treatment failure due to the development of drug resistance in the *P. falciparum*, so as an alternative ACT (Artemesin combined therapies) has been introduced in the high burden states for the treatment of *P. falciparum* [31].

Malaria control strategies in India are either early detection and prompt treatment (EDPT) or vector control [22]. Under EDPT, early treatment of malaria is done so as to minimise transmission from the diseased. Drug Distribution Centres (DDCs) and Fever Treatment Depots (FTDs) have been established in the rural areas for providing easy access to anti-malarial drugs to the community [22]. For chloroquine resistant malaria, alternative drugs are recommended. Under vector control, many strategies are followed such as, chemical control (use of indoor residual spray, uise of larvicides, malathion fogging during intense disease outbreaks),

biological control (use of biological agents for vector control), personal prophylactic measures (use of mosquito repellent creams and coils, proper covering of exposed human parts, screening of house with wire meshes), community participation (spreading awareness within the community for detection of *Anopheles* breeding places and their elimination), environmental measures (source reduction of mosquito breeding habitats) and monitoring and evaluating the programme by state national program officers or different malaria research institutes [22].

Malaria not only causes significant rates of morbidity and mortality but it is also responsible for the downfall of the productivity, agriculture & economic status of a country if left uncontrolled [24]. Malaria decreases the economic growth of a country by more than one percent point per year in endemic countries. Malaria transmission season (vector mosquito's flourishing season) coincides most of the time with the harvesting season and periods of illness during this productive time of the year proves very depressing on the world's poorest regions (UN millennium project 2005). Despite of recent advancements in diagnostic and treatment facilities throughout the world, malaria still remains a public health concern in developing countries particularly in resource poor regions [3]. By undermining the health and working capacity of hundreds of millions, it ultimately results into poverty and halts social and economic development [6]. Unlike Africa, where most of the deaths (associated to malaria) are reported in infants and children, in India, malarial mortaility has been observed to occur maximally in the age groups of 15-44 years *i.e.* economically productive age group [27], thereby affecting the economy of the country drastically. It has been reported that the total economic burden imposed by malaria in India could be around US$ 1940 million, the major burden attributable to lost earnings (75%), while rest from costs of treatment [32]. In India, most affected areas remain the poverty stricken tribal, hilly and forest fringe ones [27]. So, to minimise the affect of malaria on the socioeconomic index of India, an efficient mosquito control strategy should be the prime concern of the involved authorities.

3.2. Dengue

Dengue is the world's most threatening and fastest growing mosquito-borne viral disease, with a 30 fold increase in disease incidence over the last 50 years putting 2.5 billion people (> 40% of the world's total population)at risk of infection worldwide and 20 million cases occurring every year in more than 100 countries [2,6]. Globally, 5,00,000 people with severe dengue require hospitalization, a huge proportion of whom are children and 2.5% of those die annually [2]. In 1953-54 a new syndrome associated with dengue appeared in the Philippines, which later spread throughout the world, unlike classical dengue, this disease affected young children causing severe illness with haemorrhage and shock, resulting in high mortality, it was termed as Dengue haemorrhagic fever (DHF) [17]. Before 1970, only nine Southeast Asian countries suffered severe dengue epidemics but in 1981 large numbers of dengue haemorrhagic fever cases began to appear in the Caribbean and Latin America. It has been predicted that dengue is

omnipresent throughout the tropics, with local differences in risk mainly attributable to degree of urbanisation and climatic parameters such as rainfall, temperature, *etc* [33]. Today, dengue is endemic in more than 100 countries mainly in, South-East Asia, Africa, Eastern Mediterranean, Western Pacific and America.

The history of dengue fever (DF) dates back to the Jin Dynasty (265–420 AD) in China, however, the first recognized epidemics occurred almost simultaneously in Asia, Africa and North America in the year 1780 [34]. Dengue virus infection in humans can lead to a range of medical manifestations, from mild fever to potentially lethal dengue shock syndrome [35]. The major challenge presented by dengue remains the presence of four serotypes of dengue virus (family Flaviviridae: DENV-1, DENV-2, DENV-3 and DENV-4) dengue. A person infected by a specific dengue serotype becomes immune to that serotype for lifetime but for other serotypes the immunity provided is for 3-4 months only, thereby enhancing the chances of secondary infection (more severe) in the same or upcoming season [33].

In India, dengue outbreaks have occurred since 1950s but the occurrence and severity of disease has raised in the last two decades [34]. In 2016, total 1,29,166 cases of dengue infection occurred causing 245 deaths [36]. Till July 2017, around 23,094 cases of dengue infection has already been registered taking 32 lives [36]. In India, the first outbreak of DHF was reported in Delhi in 1988 [37], prior to which, transmission of all four dengue serotypes had already been established [38]. The trend of dengue fever in the country has been very complex and has changed considerably over past six decades in terms of prevalent serotypes, disease severity and infected geographical locations [35]. Paediatric cases of dengue haemorrhagic fever in India have a considerably higher mortality than other age groups [34]. In India, the appearance of DHF were reported for the first time in Calcutta in 1963, during this outbreak both the dengue and Chikungunya, viruses were reported to circulate together [39]. Since then several dengue outbreaks have been reported throughout the different parts of country with manifestations of haemorrhagic symptoms in varying intensities [17]. In India, dengue is widespread and endemic in 15 states, namely, Andhra Pradesh, Goa, Gujarat, Haryana, Karnataka, Kerala, Madhya Pradesh, Maharashtra, Punjab, Rajasthan, Tamil Nadu, Uttar Pradesh, West Bengal, Chandigarh, Delhi and one union territory namely Puduchery [36]. Earlier, the presence of *Aedes* mosquito in southern India was very scarce and so was the incidence of dengue but with the introduction of piped water supply, dengue made its entry to rural areas of south India and disease outbreaks occurred [40].

There are currently no licensed vaccines or specific therapeutics for dengue and constant vector control efforts could not stop the increasing incidence of dengue fever epidemics and expansion in the geographical range of endemic transmission [41]. For dengue, the reccommended treatment is replacement of plasma losses, correction of electrolyte and metabolic disturbances and blood transfusion. For vector control, following measures are followed in

India: i) personal prophylactic measures: use of mosquito repellent tools, use of bed nets *etc*, ii) Biological control: use of biocides and larvivorous fishes, iii) chemical control: use of larvicides and aerosol spray, iv) environmental management and source reduction: identification and management of mosquito breeding sources, v) Health education: imparting knowledge to common people regarding the disease and vector through various media sources, vi) community participation: involving the community for detection of *Aedes* breeding places and their elimination [36].

The high rates of mortality and morbidity associated with each dengue outbreak leads to great socio-economic impact. Dengue is an extremely expensive disease, estimated to cost the global economy over US$39 billion in 2011 only. Costs subjected in managing a group of dengue patients (serologically confirmed) at a tertiary-level private hospital in north India is quite high. The average cost of treatment per hospitalised dengue patient was estimated to be US$432.2 [42]. The mean total economic burden of dengue (loss of economic activities due to loss of workdays, the proportion requiring transfusion, deaths *etc*) was estimated to be US$27.4 million [42]. Moreover, Costs incurred in the private heath sector prove to be almost four fold higher than that of public sector expenditures. Significant economic losses are incurred by developing countries like India during each dengue epidemic [42].

The control and prevention of dengue outbreaks depend upon the proper survelliance of the disease (in order to ensure efficient and timely management of disease cases) and vector surveillance (for the effective and timely implementation of dengue vector control measures) [43]. For planning and implementation of effective public health prevention and control measures and targeting of future vaccination campaign, the knowledge on demographic differences in infection rates and severity of dengue may prove very important [44]. To minimise the illness duration and related complications, it is a must to devise effective diagnostic strategy for early diagnosis of the disease [43].

3.3. Chikungunya

Chikungunya, an arboviral disease is transmitted by culicine mosquitoes *i.e. Ae. aegypti, Ae. albopictus* and *Ae. polynesiensis*, although *Culex* has also been reported to transmit the virus in some cases [45]. This fever was first reported in Tanzania in 1952 [46,47] and the responsible pathogen, Chikungunya virus (CHIKV) belonging to the genus *Alphavirus* and the family Togaviridae was subsequently isolated in Tanzania in 1953 [47]. Epidemics were subsequently noted in the Philippines (1954, 1956 and 1968), Thailand, Cambodia, Viet Nam, India, Myanmar and Sri Lanka [48]. This specifically tropical disease is characterised by fever, rash, and incapacitating arthralgia [49]. Chikungunya, affects all age groups but severe manifestations (Persisting arthralgia, neurological syndromes and non-neurological manifestations) are more often seen in children. Chikungunya is believed to have originated in Africa, in a cycle

involving wild mammals and forest dwelling mosquitoes [50], subsequently it was introduced in Asia where it is transmitted from human to human mainly by *Ae. aegypti* and secondarily by *Ae. albopictus*.

The start of Chikungunya outbreaks dates back to the 1960s and infection rates revolved around sporadic cases until a resurgence in 2006 [34]. Resurgence of chikungunya has been linked to various factors including globalization, increased growth of vector population, loss of herd immunity and the mutation increasing the CHIKV infectivity for *Ae. albopictus* [51]. Chikungunya occurs mainly in Africa and Asia, including the Indian sub-continent, since 2005, Southeast Asian countries, namely, India, Indonesia, Maldives, Myanmar, and Thailand have reported over 1.9 million chikungunya infections [2]. In 2016, 64,057 Chikungunya infection took place in India [52].

The entry of chikungunya virus in India is not clearly known, yet Calcutta sea and air roots may be the probable entry points in India [46]. Major Indian epidemics of chikungunya were reported firstly in Calcutta (presently Kolkata) in 1963, subsequently in Pondicherry, Tamil Nadu, Andhra Pradesh, Madhya Pradesh and Maharashtra in 1965 and again in Maharashtra in 1973 [53]. In the 1963-1964 outbreak of Calcutta and 1965 outbreak of Chennai more than 3,00,000 people were affected. After a gap of 32 years this disease again appeared affecting 13 states in 2005 causing 1,400,000 infections of chikungunya during 2006 and the responsible vector species was reported to be *Ae. aegypti* [49]. The reasons for the re-emergence of chikungunya on the Indian subcontinent, and its exceptional incidence rate may be explained by increased tourism, CHIKV inoculation in a naive population and viral mutation [49].

Chikungunya virus usually shows a periodicity with occurrence of disease in the community with an interval of 3-4 years [46].The intra-outbreak studies, point towards recent mutations/changes in the viral genome enhancing the pathogenecity and enabling rapid spread [46]. Transmission of chikungunya during birth can result in neurologic, hemorrhagic, and myocardial complications for the baby or even spontaneous abortions. Mosquito vectors of chikungunya have very recently spread to Europe and the Americas, thereby enhancing the chances of disease outbreaks in those areas. This disease has already been observed for the first time in Italy in 2007 and in Carribean in 2012.

The characterstic feature of chikungunya disease is a prolonged arthralgia, *i.e.* severe joint pain, the pain associated with CHIKV infection of the joints typically persists for weeks or months causing serious economic and social impact on both the individual and the affected communities [54].

3.4. Filariasis

Lymphatic filariasis, the second most common vector borne parasitic disease is caused by the nematode *Wuchereria bancrofti* (transmitted by *Culex* mosquitoes), *Brugia malayi and Brugia timori* (transmitted by *Mansonia* mosquitoes). Both the above mentioned parasites produce similar clinical manifestations of the disease, related to the lymphatic system [55]. In India, 99.4% cases are caused by *Wuchereria bancrofti* whereas only 0.6% is caused by *Brugia malayi* [56]. The worst symptom of this chronic disease appear in adults, *i.e.* damage to the lymphatic system, arms, legs or genitals with significant pain, loss of productivity *etc.* This disease is found in 81 countries belonging to tropical and subtropical areas [57]. An estimated 120 million people in 73 countries are currently infected with filariasis. Southeast Asia accounts for around 63% (876 million) of the total people living in filarial endemic areas (1.39 billion) [2] . Southeast Asia contributes around 57% of the total global burden of 5.1 million disability-adjusted life years (DALY) lost due to lymphatic filariasis [6]. Around 40 million people are reported to suffer from long term complications of the disease [58].

WHO has targeted this disease for elimination through mass drug administration (MDA). The effectiveness of which depends on the consumption of the drug by the population. This strategy (MDA) alone has been shown to suppress transmission of lymphatic filariasis quite efficiently but it is often accompanied by resurgence once there is residual infection in the population. So, ideal control of lymphatic filariasis can be achieved only through integration of different strategies of vector control along with MDA [59].

India is the largest filaria endemic country of the world. A National Filarial Control Programme (NFCP) was launched in 1955, which currently covers a population of 40 million people with a strategy of selective chemotherapy (mass diethylcarbamazine administration) [60]. In India, filariasis are endemic in 17 states and 6 union territories putting about 650 million people at the risk of infection [55]. The National Health policy (2002) envisaged elimination of lymphatic filariasis in India by 2015 through strategies mainly, i) Annual mass drug administration (MDA of single dose of DEC (Diethylcarbamazine citrate) and Albendazole ii) home based control of lymphoedema cases and up-scaling of hydrocele operations [56]. To follow the above goals, the Government of India in 2004 launched nationwide MDA programme in endemic areas as well as home based morbidity management, scaling up hydrocelectomies. During 2004, only 202 districts could be covered with a coverage rate of 72.6%. In 2007, all the 255 known lymphatic filariasis endemic districts were brought under MDA. The population coverage during MDA improved from 72.6 % in 2004 to 89% in 2015, resulting in reduction of microfilaria rate from 1.2% in 2004 to 0.3% in 2015 [56]. As per WHO guidelines (2011), districts conducting minimum five rounds of MDA with more than 65% population coverage are subjected to Transmission Assessment Survey (TAS) for presence of circulating antigenemia in children born after initiation of MDA to unveil the current infection status, needed to

take decision for MDA stoppage [56]. Till May 2016, 72 districts (each with approximately 164 million population) qualified for stoppage of MDA [56]. Since 2004, 1,41,902 hydrocele operations have been reported form India [56]. Some states have started paying attention to home based foot hygiene practices for management of lymphodema cases [56].

Filariasis is a disease of poor and it is reported as a cause and effect of Poverty [60]. Poor hygiene and sanitary facilities with low socioeconomic status of the community provide the ambience ideal for vector mosquito breeding and thus transmission of the causative pathogen [57]. It has been reported that the annual economic loss due to filariasis in India is US$ 1 billion and US$5.3 billion from blinding trachoma and substantial reductions in future wage earning capacity as a result of chronic hookworm infection in childhood [61]. Besides disability, this disease causes personal trauma to the affected persons and its long term suffering leads to social exclusion.

3.5. Japanese encephalitis

Japanese encephalitis (JE), one of the major public health disease was identified as a clinical issue in Japan in 1971 and in the past decades it has spread to many countries of Southeast Asia and parts of Western Pacific region [62]. JE is basically an infection of the brain and children are more vulnerable to this infection and inflammation of the brain. The infection with JE virus can range from non specific febrile illness to meningiencephalomyelitis illness [62]. While most JE virus infections are mild or asymptotic, approximately 1 in 250 infections results in severe disease [2]. Around 60 % of the world's population *i.e.* 3 billion people inhabit JE endemic regions [63]. JE is endemic mainly to rural areas with rice plantations, pig rearing, high temperature, rainfall and relative humidity (rainwater clogged rice fields serve as the the breeding sites for vector mosquitoes whereas pigs acts as the reservoir of virus), putting 1.9 billion people at risk of JE infection [64]. Japanese encephalitis is a principal cause of disability among the paediatric and rural people in Asia. In Asia, around 68,000 clinical cases of JE infections are reported to occur annually causing 5-35% deaths and 75% JE related disability rate [2].

In India, the first incidence of JE was reported in 1955 in Tamilnadu and neighbouring districts of Andhra Pradesh. Annually around 35000-50000 cases of JE infection are reported, of which 30-50 % individuals face neurological infection whereas 20-40% die [65]. Since 1972, JE has expanded its range and has spread to West Bengal, Uttar Pradesh, Assam, Manipur, Bihar, Andhra Pradesh, Pondicherry, Karnataka, Goa, Kerala and Maharashtra. This cycle consists of pigs (major reservoir / amplifying host), water birds (carriers) and mosquitoes (vectors). The *Culex vishnui* subgroup of mosquitoes had been established as major vectors of JE. India faced its first major JE outbreak in 1973 in districts of West Bengal causing 300 deaths [66]. In 2016, total 444 cases of JE were reported causing 60 deaths [67].

Though there is no specific antiviral medication available for treatment of JE infection, but the availability of JE vaccination (developed by Central research institute, Kasauli) [67] appears to be the best control measure in JE endemic areas. In JE endemic areas, the immunization of JE vaccine is included in the general immunization schedule. Also, immunization of pigs and locating piggeries away from human dwelling is also a preventive measure.

The prevalence of JE is higher in countries that have lower socioeconomic status, than more prosperous neighbouring countries, indicating the involvement of economic and social strength as an additional risk factor that affects the rate of JE transmission and prevalence in non-immune populations [64]. A principal part of India's economy depends on agriculture, and the presence of JE vectors breeding sites in agricultural land increases the chances of the poor farmer getting infected by JE virus, there by affecting both the economical and social indices of the country.

3.6. Zika

Zika virus (genus Flavivirus, family Flaviviridae) is an emerging arbovirus of public health importance transmitted by *Aedes* mosquito. This virus is closely related to other flaviviruses of public health importance such as dengue fever, chikungunya and yellow fever [68]. Zika virus was first isolated in Uganda, in 1947 and for many years, the virus sustained on earth causing sporadic human infections in Africa and Asia [69]. Since 2013, cases and outbreaks of this disease have been reported from the Western Pacific, Africa, Asia and latin Americas and as of now, zika infection have been reported from 70 countries [70]. Most people infected with zika are mostly asymptomatic however clinical manifestations ranging from mild fever, skin rashes, joint pain, low-grade fever, conjunctivitis, to severe neurological disorders, microcephaly, and Guillain-Barré syndrome may take place [71]. There are evidences relating ZIKV and severe neurological disorders during prenatal development [72]. The recent reports about the sexual transmission route of Zika, changes in the epidemiology, possible links with microcephaly cases and other neurological disorders have rapidly changed the risk profile of the disease pushing WHO to declare it as a 'Public Health Emergency of International concern' [70]. With three confirmed cases of zika in India and unavailability of either vaccination or treatment medications against zika, India stands at a very high risk of ZIKV infection and related socioeconomic disturbances in the near future.

4. Present Control Strategies for Mosquito Borne Diseases

The control strategies for mosquito borne diseases can be divided into two groups: 1. Diseases against which vaccination or therpeutic treatment is available, 2. diseases which have no available vaccine or medications. For the first group, both disease prevention by vaccination or early diagnosis followed by medication and control of vector population is sought. Whereas, for the second group the sole available approach remains minimising the infection

rate through vector control.

4.1. Prevention by vaccination

This strategy is followed for Japanese encephalitis. In last few decades through vaccination JE has been eliminated from Japan, Taiwan, China and Korea [73]. Three types of vaccines are used throughout the world:

i) Formalin inactivated mouse brain derived vaccine,

ii) Inactivated primary hamster kidney cell derived vaccine,

iii) Cell culture derived attenuated vaccine.

Of the above only the first one is WHO approved. Three doses of this vaccine (produced by Centre for Research, Kasauli) provide immunity for few years) [67]. JE vaccination was started in India in 2006. Large JE vaccination campaigns were carried out in 2006 (11 districts), 2007 (27 districts), 2008 (22 districts), 2009 (30 districts) [74]. In 2011, The JE vaccine was introduced in the routine immunization under Universal Immunization program in 181 JE endemic districts at a single dose at 16-18 months at the time of 1st booster of DTP vaccine. In 2013, another dose of the vaccine was added at 9 months age along with measles vaccine [74]. Till 2015, 155 JE endemic districts have been covered under JE campaign and approximately, 10.8 crore children have received the vaccination through campaigns [74]. Afterwards, JE vaccination campaigns for adults were conducted owing to outnumbering of pediatric JE infection by adult infection rates [74].

4.2. Anti pathogen measure

It is adopted for lymphatic filariasis and also for malaria caused by *P. vivax*. In case of Filaria, annual mass administration of single dose of DEC (Diethylcarbamzine, an anti filarial worm medication) and albendazole is done to interrupt the transmission of the disease [56]. For malaria, after early diagnosis, chloroquine is administered as an anti malarial drug. However due to increased chloroquine resistance often a combined drug therapy is followed.

However the above two strategies can suppress the disease, but strategies combined with Vector control is often adopted for efficient disease prevention and transmission.

4.3. Vector control

Majority of mosquito borne diseases *i.e.* malaria, dengue, chikungunya *etc* do not have available vaccine or safe medications, so the sole method to decrease their infection rate is to cut down the number of vector population responsible for the transmission of disease causing pathogen, thereby obstructing the transmission cycle [75]. Since long time ago, vector control

has been used throughout the world.

Adult vector control: The history of vector control in India can be divided into two phases: before and after the discovery of DDT. Before 1936, various control methods *i.e.* biological, mechanical and chemical had been employed for mosquito control such as the application of larvivorous fish (eg. Gambusia, Guppy) to the mosquito breeding habitats, use of oils and Paris green in breeding sites and the provision of a suitable drainage system [76]. A significant decrease in the malaria vector population was observed in Bombay city through the application of above mentioned measures along with implementation of legislative measures, where *An. stephensi* breeding was observed in water tanks, wells, cisterns *etc* [15]. Observing the success by spray of pyrethrum extract inside the houses to kill the adult mosquitoes in South Africa, mosquito control trials were undertaken in human dwellings and cattle sheds in some part of India [15].

DDT was discovered in the year 1939 by Paul Mueller who later became a Nobel laureate for the same [77]. On an experimental basis, it was introduced in the Assam-Burma front in the army camps of world war II as a residual insecticide in mosquito control programme with great results [78]. Afterwards, few more successful experiments, DDT was accepted as an indoor spray as the control measure against malaria [15]. In 1950, another insecticide Benzene hexachloride (BHC) was used in Assam [79]. In the year 1953, National Malaria Control Programme (NMCP) was launched which had a remarkble impact on the malaria situation in the country, also was noted a significant decrease in the malarometric indices [26]. During 1980s, insecticides belonging to synthetic pyrethroid group were introduced in the public health programmes. Deltamethrin was introduced in a trial and was found effective for vectors as residual insecticide [15]. Successively, synthetic pyrethroids such as cyfluthrin, lambda cyhalothrin were introduced into public health programmes; currently all three above mentioned synthetic pyethroids are in use both as indoor residual spray and as impregnated on mosquito nets along with some personal protective measures [15]. However, varying degree of insecticide resistance has been observed in different mosquito vectors throughout India [10,12,80-83].

Larval vector control: Destruction of larval habitats (sealing of water holding vessels), designing of a proper drainage system and spray of insecticide against larva include the major aspects of larval management in India. For mosquito larval control, temephos is the most preferred larvicide, also recommended by both WHO and National Vector Borne Disease Control Programme, India (NVBDCP).

5. Major Constraints in Mosquito Borne Disease Control

5.1. Drug resistance

With the use of drugs and medications for the treatment of infection, the pathogen sub-

sequently develops resistance against the medication used, this is referred to as drug resistance. The *P. falciparum* resistance against chloroquine has resulted in increased malaria mortality and morbidity throughout the world [84]. Despite the worldwide spread of resistance, chloquine still remains the first line treatment for malaria [85]. Studies in African countries have reported a 2-3 fold increase in malaria death and approximately 6 fold higher malarial mortality in children attributable to emergence of chloroquine resistance [85]. *P. falciparum* has also developed resistance against artemisin derivatives [58]. Antimalarial drug resistance usually confers a fitness disadvantage upon the malaria parasites, but parasites in the Southeast Asian region have been exposed to several different selective forces which has created a genetic background that may predispose to the emergence of resistance [86]. WHO now recommends ACTs as the suitable treatment for uncomplicated *P. falciparum* malaria however, it will be terrible if artemisinin resistance reaches regions carrying the bulk of malaria, *i.e.* India and Africa [87]. Such drug resistance pose a huge challenge against malaria eradication worldwide.

Similar resistance has also been reported against anti filarial drug DEC and albendazole in *W.bancrofti* [88]. It has been noted that benzimidazole resistance is widespread in a number of nematodes of veterinary importance [89].

5.2. Insecticide resistance

Continuous use of synthetic insecticides under vector control programmes has given rise to a new phenomenon known as Insecticide resistance in many mosquito vector species [90]. This term refers to the selection of insecticide resistant populations of the vector mosquito under insecticide selection pressure. According to the World Health Organization (WHO), resistance is defined as the ability of an insect to withstand the effects of an insecticide by becoming resistant to its toxic effects by means of natural selection and mutations [91]. While Insecticide Resistance Action Committee (IRAC) defines resistance as a heritable change in the sensitivity of a pest population that is reflected in the repeated failure of a product to achieve the expected level of control when used according to the label recommendation for that pest species [92]. Appropriate tools (biological, biochemical and/or molecular) are needed to identify the mechanisms involved at individual or population levels [93]. Insecticide resistance is an increasing problem faced by those who need insecticides to efficiently control medical, veterinary, agricultural insect pest [93]. Resistance is a heritable character that relies on a genetic basis. Resistance results from the selection of a genetic modification in one or several genes occurring by migration or mutation [94].

The use of insecticides for agricultural purposes and more recently for public health has played pivotal step in the selection of resistance in mosquitoes [95]. Resistance involves several physiological and behavioural changes. Changes in the insecticide target site that reduce its binding to insecticides (known as target site resistance) is the best understood type of resis-

tance mechanism [96], enhanced insecticide metabolism that lowers the amount of insecticide reaching the target site (known as metabolic resistance) is more complex but recent advances have identified key enzymes responsible for insecticide detoxification [97]. Other physiological changes (e.g. reduced penetration through cuticle, *i.e.* cuticular resistance) and behavioural changes in the mosquito population have also been identified. The major mechanism that enables insects to grow resistance against insecticide can be divided into four categories: Behavioral avoidance, reduced penetration, metabolic resistance and target site insensitivity; the latter two being the major resistance mechanism occurring in insects. Metabolic resistance is caused due to the elevated activities of digestive/detoxification enzymes which help in the detoxification of foreign compounds [90]; enzyme groups mainly related to this task are Esterases, Monooxygenases and Glutathione-S-transferases [98]. While, target site insensitivity refers to the modification within the nervous system of a specific site where the insecticide binds [99].

Resistance management is therefore a major challenge for vector control programme in countries like India where there is a prevalence of vector borne diseases [80]. A detailed knowledge of the major factors behind insecticide resistance is the immediate need for implementation of safer and efficient vector control programmes [90].

6. Integrated Vector Management

Integrated Vector Management is defined (by WHO) as a rational decision-making process for the optimal use of resources for vector control [100]. The main driving force behind the IVM movement is the need to overcome the challenges or limitations associated with conventional single intervention approaches to vector control. Integrated vector management aims to improve the efficacy, cost-effectiveness, ecological soundness and sustainability of vector control [101]. IVM entails the use of a range of interventions, alone or in combination, in order to implement a more cost-effective control and reduce dependence on any single intervention. This strategy also serves to extend the useful life of insecticides and drugs by reducing the selection pressure for resistance development [101]. IVM has been shown to delay onset of behavioural resistance [102].

An IVM approach takes into account the available health infrastructure and resources and integrates all available and effective chemical, biological or environmental measures. It also encourages effective coordination of other important sectors that have an impact on vector borne diseases, such as, health, water, solid waste and sewage disposal, housing and agriculture [101]. An IVM approach is evidence-based and it has the capacity to generate local data on disease epidemiology and vector ecology. The key elements of IVM are [100]: i) Advocacy, regulatory control and social mobilization, ii) Collaboration between the health sector and other sectors to make optimal use of resources, and improve planning and decision-making,

iii)Integration of non-chemical with chemical vector control methods, and integration of vector control with other disease control measures which target the parasite or pathogen, iv) Evidence-based decision making which is guided by operational research and entomological and epidemiological surveillance and evaluation, v) Development of adequate human resources, training and career structures at national and local level to enhance capacity and management of IVM programmes.

IVM is guided by the following basic principles: 1) to effectively reduce adult vector populations and pathogen transmission; 2) that interventions should be ecologically, environmentally, socially, economically and politically acceptable; 3) that management strategies should not create adverse side effects such as environmental contamination or the development of resistance, nor should they have a negative impact on non-target organisms, including beneficial insects, humans, domestic animals and wildlife; 4) to understand the transmission cycle, the life history of the vector species, and the natural factors regulating vector survivorship are critical; 5) that the most effective programmes develop descriptive and predictive models for population dynamics and transmission potential; 6) to have flexibility in terms of changing strategies and tools in response to surveillance and biological data; and 7) that management strategies should be dynamic and able to respond to the results of an active and sensitive mosquito/pathogen surveillance programme [103].

The success of IVM programmes are the integrated control of malaria in the Zambian Copper Belt in the 1930s and 1940s, the initiative against Chagas disease vectors in Latin America, and the Onchocerciasis Control Programme in West Africa since the 1970s. These success stories demonstrate that strategically effective, well-coordinated and sustained initiatives can bring extraordinary benefits in health and socioeconomic development [101]. The above mentioned programme could achieve their target owing to the use of efficient systems for monitoring, evaluation and reporting and ii) procedures for the rapid identification and correction of problems [101]. The adoption of a strategy for IVM provides new opportunities for effective action against vector borne disease.

7. Conclusion

To overcome the burden disposed on India by mosquito borne diseases, the only available approach is implantation of effective vector control strategy. An efficient vector control depends on proper planning which in turn depends on investigation before the planning of strategy. For treatment of disease with the use of medication, the major challenge is to minimise drug resistance, similarly for vector control, it is to halt the development of insecticide resistance. For combating drug resistance, the prime concern should be taking medications only under medical supervision, completion of course of medication and safe disposal of medicines. For insecticide resistance, the best way is to manage the level of insecticide resistance

within the vector population; this can be done through insecticide resistance management (IRM) [94]. For IRM, the first approach should be to monitor the level of resistance developed within the target species at a local level, so that site specific effective insecticide dosage can be devised. The alteration in behaviour of the target species should be studied to keep a check of behavioural modification taking place (if any). Constant use of insecticides belonging to same chemical group should be avoided, instead a rotation of different insecticide group should be followed while spraying [94]. Also, insecticide use should be limited both in space and time dimension, *i.e.* only those sites where insecticide usage is needed/inevitable for public health security, should be brought under vector control programmes using insecticide. There should always be a time period gap between successive sprays. Low doses of insecticide should be used to maintain the population of of susceptible strains [104]. Insecticide that persist in the environment for a very small time should be used, thereby reducing the selection pressure [104]. The mechanisms behind insecticide resistance should be thoroughly studied and methods to block such mechanisms (through enzyme blockers, synergists *etc*) should be sought for. Also research assignments on formulation of novel insecticidal compounds with novel targets, search for compounds of botanical origin with such potentiality, sterile male mosquito technology, biological control of mosquito, etc should be devised for sustainable, environment friendly and effective disease control. Lastly, public awareness regarding mosquito breeding habitats and source reduction by public health educational campaigns to reduce backyard mosquito larval habitats (*i.e. Anopheles, Aedes, Culex*) should be conducted on a regular basis. Community participation can help reduce mosquito habitats, while developing long term, low cost sustainable programs. In the event of public health emergency, community peer educators can both help in the reduction of vector habitats and provide assurance to the community regarding mosquito control programs.

8. References

1. Gubler DJ. Resurgent vector-borne diseases as a global health problem. Emerging infectious diseases. 1998; 4(3): 442.

2. World Health Organization. A global brief on vector-borne diseases. 2014; DCO/WHO/2014.1: 1-56.

3. Kumar V, Mangal A, Panesar S, Yadav G, Talwar R, Raut D, Singh S. Forecasting malaria cases using climatic factors in Delhi, India: a time series analysis. Malaria research and treatment. 2014; 1: 1-6.

4. Gubler DJ. Insects in Disease Transmission. In: Strickland GT, editor. Hunter tropical medicine, 7th edition. Philadelphia (PA): W. B. Saunders. 1991; 981-1000.

5. Gubler DJ. Vector-borne diseases. Revue scientifique et technique. 2009; 28(2): 583.

6. World Health Organization. Global vector control response 2017-2030. 2017; 1-64.

7. World Health Organization. “Mosquitoes and other biting dipterans” in Vector control Methods for use by individuals and communities. 1997; 7-177.

8. Gould EA, Solomon T. Pathogenic flaviviruses. The Lancet. 2008; 371(9611): 500-509.

9. Tolle MA. Mosquito-borne diseases. Current problems in pediatric and adolescent health care. 2009; 39(4): 97-140.

10. Dhiman RC, Pahwa S, Dhillon GP, Dash AP. Climate change and threat of vector-borne diseases in India: are we prepared?. Parasitology Research. 2010; 106(4): 763-773.

11. Epstein PR, Diaz HF, Elias S, Grabherr G, Graham NE, Martens WJ, Mosley-Thompson E, Susskind J. Biological and physical signs of climate change: focus on mosquito-borne diseases. Bulletin of the American Meteorological Society. 1998; 79(3): 409-417.

12. Bharati M, Saha D. Insecticide susceptibility status and major detoxifying enzymes activity in Aedes albopictus (Skuse), vector of dengue and chikungunya in Northern part of West Bengal, India. Acta Tropica. 2017; 170: 112-119.

13. Cousins S. Three Zika cases are found in India after random tests. BMJ 2017; 357: j2654.

14. Dev V, Sharma VP. The dominant mosquito vectors of human malaria in India. In Anopheles mosquitoes-New insights into malaria vectors 2013. InTech.

15. Anonymous. Chemical insecticides in malaria vector control in India. ICMR Bulletin. 2002; 32: 1-7.

16. Paupy C, Delatte H, Bagny L, Corbel V, Fontenille D. Aedes albopictus, an arbovirus vector: from the darkness to the light. Microbes and Infection. 2009; 11(14): 1177-1185.

17. Kalra NL, Kaul SM, Rastogi RM. Prevalence of Aedes aegypti and Aedes albopictus-Vectors of Dengue Haemorrhagic Fever in North, North-East and Central India. WHO Dengue Bulletin. 1997; 21: 84-92.

18. Fakooziba MR, Vijayan VA. Seasonal abundance of larval stage of Culex species mosquitoes (Diptera: Culicidae) in an endemic area of Japanese encephalitis in Mysore, India. Pakistan J Biol Sci. 2006; 9: 2468-2472.

19.Barbosa RM, Souto A, Eiras AE, Regis L. Laboratory and field evaluation of an oviposition trap for Culex quinquefasciatus (Diptera: Culicidae). Memórias do Instituto Oswaldo Cruz. 2007; 102(4): 523-529.

20. Chakraborty MS, Chakravarti SK, Mukherjee KK, Hati AK. Isolation of Japanese encephalitis (JE) virus from Mansonia annulifera species of mosquito. Journal of the Indian Medical Association. 1980; 75(10).

21. Sharma VP. Fighting malaria in India. Current Science. 1998; 75(11): 1127-1140.

22. National Vector Borne Disease Control Programme, NVBDCP malaria. 2017.

23. Bhattacharya S, Sharma C, Dhiman RC, Mitra AP. Climate change and malaria in India. Current Science-Bangalore-. 2006; 90(3): 369.

24. Parida SP, Bhatia V. Malaria status in India with focus on Odisha State having maximum disease burden. Global Journal of Medicine and Public Health. 2015; 4(5): 1-6.

25. Sharma VP. Current scenario of malaria in India. Parassitologia. 1999; 41(1-3): 349-353.

26. Sharma GK. Review of malaria and its control in India. In V.P. Sharma, Proceedings of Indo-UK Workshop on Malaria, Malaria Research Centre, Delhi. 1984; 13.

27. Kumar A, Valecha N, Jain T, Dash AP. Burden of malaria in India: retrospective and prospective view. The American journal of tropical medicine and hygiene. 2007; 77(6_Suppl): 69-78.

28. Nagpal BN, Sharma VP. Indian Anophelines. Oxford & IBH Publishing Co. Pvt. LTD.; New Delhi (ISBN 81-204-0929-9). 1995; 416.

29. Sharma RK, Thakor HG, Saha KB, Sonal GS, Dhariwal AC, Singh N. Malaria situation in India with special reference to tribal areas. The Indian journal of medical research. 2015; 141(5): 537.

30. Anonymous, Operational manual for malaria elimination in India version 1, Directorate of National Vector Borne Disease Control Programme Directorate General of Health Services Ministry of Health & Family Welfare Government of India. 2016; 1-256.

31. Dash AP, Valecha N, Anvikar AR, Kumar A. Malaria in India: challenges and opportunities. Journal of biosciences. 2008; 33(4): 583-92.

32. Gupta I, Chowdhury S. Economic burden of malaria in India: The need for effective spending. WHO South-East Asia Journal of Public Health | January-March. 2014; 3 (1): 95-102.

33. Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL, Drake JM, Brownstein JS, Hoen AG, Sankoh O, Myers MF. The global distribution and burden of dengue. Nature. 2013; 496(7446): 504.

34. Cecilia D. Current status of dengue and chikungunya in India. WHO South-East Asia Journal of Public Health. 2014; 3(1): 22-27.

35. Gupta N, Srivastava S, Jain A, Chaturvedi UC. Dengue in India. Indian Journal of Medical Research. 2012; 136: 373-390.

36. National Vector Borne Disease Control Programme, NVBDCP dengue. 2017. www.nvbdcp.gov.in/dengu1 retrieved on 11.07.2017.

37. Kabra SK, Verma IC, Arora NK, Jain Y, Kalra V. Dengue haemorrhagic fever in children in Delhi. Bull World Health Organ. 1992; 70 : 105-108.

38. World Health Organization. Dengue haemorrhagic fever: diagnosis, treatment, prevention and control. Geneva: WHO. 1997.

39. Sarkar JK, Chatterjee SN, Chakravarty SK. Three-year study of mosquito-borne haemorrhagic fever in Calcutta. Transactions of the Royal Society of Tropical Medicine and Hygiene. 1967; 61(5): 725-735.

40. Kader A, Fernando J, Kiruba J, Palani G, Sarangapani TD, Kandasamy P, Appavoo NC, Anuradha L. Investigation of Aedes aegypti breeding during dengue fever outbreak in villages of Dharampuri district, Tamil Nadu, India. Dengue Bulletin. 1998; 22.

41. Tatem AJ, Hay SI, Rogers DJ. Global traffic and disease vector dispersal. Proceedings of National Academy of SAciences U.S.A. 2006; 103: 6242–6247.

42. Garg P, Nagpal J, Khairnar P, Seneviratne SL. Economic burden of dengue infections in India. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2008; 102(6): 570-577.

43. Sharma SN, Raina VK, Kumar A. Dengue/DHF: an emerging disease in India. The Journal of communicable diseases. 2000; 32(3): 175-179.

44. Chakravarti A, Arora R, Luxemburger C. Fifty years of dengue in India. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2012; 106(5): 273-282.

45. Lahariya C, Pradhan SK. Emergence of chikungunya virus in Indian subcontinent after 32 years: a review. Journal of vector borne diseases. 2006; 43(4): 151.

46. Robinson MC. An epidemic of virus disease in southern province, Tanganyika territory, in 1952-53. Transactions of the Royal Society of Tropical Medicine and Hygiene. 1955; 49(1): 28–32.

47. Ross RW. The Newala epidemic III; the virus: isolation, pathogenic properties and relationship to the epidemic. Journal of Hygiene. 1956; 54: 177–191.

48. Pastorino B, Muyembe-Tamfum JJ, Bessaud M, Tock F, Tolou H, Durand JP, Peyrefitte CN. Epidemic resurgence of Chikungunya virus in Democratic Republic of the Congo: identification of a new central African strain. Journal of

Medical Virology. 2004; 74: 277–282.

49. Pilaoux G, Gauzere BA, Jaureguiberry S, Strobel M. Chikungunya, an emerging arboviruses. 2007; 7(5): 319-327.

50. Brooks GF, Butel JS, Morse SA. Human arboviral infections. In: Jawetz, Melnick and Adelberg's Medical microbiology. 23rd edn. Singapore: Mc Graw Hill. 2004: 514–524.

51. Diallo M, Thonnon J, Traore Lamizana M, Fontenille D. Vectors of Chikungunya virus in Senegal: current data and transmission cycles. American Journal of Tropical Medicine and Hygiene. 1999; 60: 281–286.

52. National Vector Borne Disease Control Programme, NVBDCP chikungunya. 2017. www.nvbdcp.gov.in/Chikun-main retrieved on 11.07.2017.

53. Sudeep AB, Parashar D. Chikungunya: an overview. Journal of biosciences. 2008; 33(4): 443-449.

54. Powers AM, Logue CH. Changing patterns of chikungunya virus: re-emergence of a zoonotic arbovirus. Journal of General Virology. 2007; 88(9): 2363-2377.

55. Raju K, Jambulingam P, Sabesan S, Vanamail P. Lymphatic filariasis in India: epidemiology and control measures. Journal of postgraduate medicine. 2010; 56(3): 232-238.

56. National Vector Borne Disease Control Programme, NVBDCP filariasis. 2017. www.nvbdcp.gov.in/filariasis-new retrieved on 11.07.2017.

57. Upadhyayula SM, Mutheneni SR, Kadiri MR, Kumaraswamy S, Nagalla B. A cohort study of lymphatic filariasis on socio economic conditions in Andhra Pradesh, India. PloS one. 2012; 7(3): e33779.

58. World Health Organisation. Global programme to eliminate lymphatic filariasis. 2010; 1-93.

59. Biradar MK, Holyachi S. Coverage and compliance of mass drug administration against lymphatic filariasis in Kalaburgi district. International Journal Of Community Medicine And Public Health. 2017; 4(7): 2502-2505.

60. Anonymous. Prospects of elimination of lymphatic filariasis in India. 2002. ICMR Bulletin 32: 5 (May-June)6 1-14.

61. Molyneux DH, Hotez PJ, Fenwick A. "Rapid-impact interventions": how a policy of integrated control for Africa's neglected tropical diseases could benefit the poor. PLoS medicine. 2005; 2(11): e336.

62. Singh A, Saxena SK, Srivastava AK, Mathur A. Japanese encephalitis: A persistent threat. Proceedings of the National Academy of Sciences, India Section B: Biological Sciences. 2012; 82(1): 55-68.

63. Joshi MV, Geevarghese G, Mishra AC. Epidemiology of Japanese encephalitis in India: NIV Pune Year Book. Orient Longman publication. 1954-2004, 308-328.

64. Samuel PP, Ramesh D, Muniaraj M, Arunachalam N. A three year longitudinal study on the seasonal Japanese encephalitis vector abundance in Thanjavur district, Tamil Nadu, India. Journal of Entomology and Zoology Studies. 2016; 4(1): 98-104.

65. Mahendra H, Yogesh G, Harish L, Monika K, Kumar S. A Recent Review: Japanese Encephalitis. World Journal of Pharmacy and Pharmaceutical Sciences. 2014; 3(3): 545-546.

66. Bandyopadhyay B, Bhattacharyya I, Adhikary S, Mondal S, Konar J, Dawar N, Biswas A, Bhattacharya N. Incidence of Japanese encephalitis among acute encephalitis syndrome cases in West Bengal, India. BioMed research international. 2013; 2013.

67. National Vector Borne Disease Control Programme, NVBDCP Japanese Encephalitis. 2017. www.nvbdcp.gov.in/je-new retrieved on 11.07.2017.

68. Cao-Lormeau VM, Roche C, Teissier A, Robin E, Berry AL, Mallet HP, Sall AA, Musso D. Zika virus, French polynesia, South pacific, 2013. Emerging infectious diseases. 2014; 20(6): 1085.

69. Kindhauser MK, Allen T, Frank V, Santhana RS, Dye C. Zika: the origin and spread of a mosquito-borne virus. Bulletin of the World Health Organization. 2016; 94(9): 675-86C.

70. Singh T. Zika virus: Can India win the fight?. Indian journal of community medicine: official publication of Indian Association of Preventive & Social Medicine. 2017; 42(2): 69.

71. Hamel R, Liégeois F, Wichit S, Pompon J, Diop F, Talignani L, Thomas F, Desprès P, Yssel H, Missé D. Zika virus: epidemiology, clinical features and host-virus interactions. Microbes and Infection. 2016; 18(7): 441-449.

72. Johansson MA, Mier-y-Teran-Romero L, Reefhuis J, Gilboa SM, Hills SL. Zika and the risk of microcephaly. New England Journal of Medicine. 2016; 375(1): 1-4.

73. Chambers TJ, Tsai TF, Pervikov Y, Monath TP. Vaccine development against dengue and Japanese encephalitis: report of a World Health Organization meeting. Vaccine. 1997; 15(14):1494-1502.

74. Vashishtha, V.M. and Ramachandran, V.G. Vaccination policy for Japanese encephalitis in India: Tread with caution!. Indian pediatrics. 2015; 52(10): 837-839.

75. Bharati M, Saha P, Saha D. Variation in Esterase Activity Among Different Aedes aegypti L. Populations from the Dooars and Terai Regions of West Bengal, India. Proceedings of the Zoological Society. 2016.

76. Johnson DR. Status of malaria eradication in India. Mosquito. News. 1965; 25: 361.

77. Russel PF. Man's mystery of Malaria, Oxford University Press. New York. 1955; 308.

78. Singh J. Activities of the Malaria institute of India during world war II. Indian Journal of Malariology. 1962; 16: 504.

79. Bertram DA. A critical evaluation of DDT and Gammaxene in malarial control in upper Assam over five years with particular reference to effect on An. minimus. Annals of Tropical Medicine and Parasitology. 1950; 44: 242.

80. Shetty V, Sanil D, Shetty NJ. Insecticide susceptibility status in three medically important species of mosquitoes, An. stephensi, Ae. aegypti and C. quinquefasciatus, from Bruhat Bengaluru Mahanagara Palike, Karnataka, India. Pest Management Science. 2013; 69: 257–267.

81. Dhiman S, Yadav K, Rabha B, Goswami D, Hazarika S, Tyagi V. Evaluation of insecticides susceptibility and malaria vector potential of Anopheles annularis sl and Anopheles vagus in Assam, India. PloS one. 2016; 11(3): e0151786.

82. Sivan A, Shriram AN, Sunish IP, Vidhya PT. Studies on insecticide susceptibility of Aedes aegypti (Linn) and Aedes albopictus (Skuse) vectors of dengue and chikungunya in Andaman and Nicobar Islands, India. Parasitology research. 2015; 114(12): 4693-4702.

83. Yadav K, Rabha B, Dhiman S, Veer V. Multi-insecticide susceptibility evaluation of dengue vectors Stegomyia albopicta and St. aegypti in Assam, India. Parasites & vectors. 2015; 8(1): 143-150.

84. Sidhu AB, Verdier-Pinard D, Fidock DA. Chloroquine resistance in Plasmodium falciparum malaria parasites conferred by pfcrt mutations. Science. 2002; 298(5591): 210-213.

85. Trape JF. The public health impact of chloroquine resistance in Africa. The American journal of tropical medicine and hygiene. 2001; 64: 12-17.

86. Miotto O, Amato R, Ashley EA, MacInnis B, Almagro-Garcia J, Amaratunga C, Lim P, Mead D, Oyola SO, Dhorda M, Imwong M. Genetic architecture of artemisinin-resistant Plasmodium falciparum. Nature genetics. 2015; 47(3): 226-234.

87. Hanboonkunupakarn B, White NJ. The threat of antimalarial drug resistance. Tropical Diseases, Travel Medicine and Vaccines. 2016; 2(1): 10.

88. Schwab AE, Churcher TS, Schwab AJ, Basanez MG, Prichard RK. Population genetics of concurrent selection with albendazole and ivermectin or diethylcarbamazine on the possible spread of albendazole resistance in Wuchereria bancrofti. Parasitology. 2006; 133(5): 589-601.

89. Mccarthy J. Is antihelminthic resistance a threat to eliminate lymphatic filariasis? The American Journal of Tropical medicine and hugiene. 2005; 73(2): 232-233.

90. Singh RK, Kumar G, Mittal PK. Insecticide susceptibility status of malaria vectors in India: A review. International Journal of Mosquito Research. 2014; 1: 5-9.

91. Davidson G. Insecticide resistance in An. sundaicus. Nature. 1957; 180: 1333-1335.

92. Anonymous. IRAC: Prevention and Management of Insecticide Resistance in Vectors of Public Health Importance In: Resistance Management for Sustainable Agriculture and Improved Public Health. 2002; 2: 72-143.

93. Hemigway J. Techniques to detect insecticide resistance mechanisms (field and laboratory manual). World Health Organization, Geneva, Switzerland. 1998.

94. Corbel V, N'Guessan R. Distribution, Mechanisms, Impact and Management of Insecticide Resistance in Malaria Vectors: A Pragmatic Review. In: S Manguin, An. mosquitoes - New insights into malaria vectors, InTech, Rijeka. 2013; 579-633.

95. Ranson H, Guessan R N, Lines J, Moiroux N, Nkuni Z, Corbel V. Pyrethroid resistance in African anopheline mosquitoes: what are the implications for malaria control? Trends in Parasitology. 2011; 27: 91-98.

96. Ridl FC, Bass C, Torrez M, Govender D, Ramdeen V, Yellot L, Edu AE, Schwabe C, Mohloai P, Maharaj R. A pre-intervention study of malaria vector abundance in Rio Muni, Equatorial Guinea: their role in malaria transmission and the incidence of insecticide resistance alleles. Malaria Journal. 2008; 7: 194.

97. Mitchell SN, Stevenson BJ, Muller P, Wilding CS, Egyir-Yawson A, Field SG, Hemingway J, Paine MJ, Ranson H, Donnelly MJ. Identification and validation of a gene causing cross-resistance between insecticide classes in An. gambiae from Ghana. Proc. Proceedings of National Academy of SAciences U.S.A. 2012; 109: 6147-6152.

98. Hemingway J, Ranson H. Insecticide resistance in insect vectors of human disease. Annual Reviews on Entomology. 2000; 45:371-391.

99. Aizoun N, Aikpon R, Akogbeto M. Evidence of increasing L1014F kdr mutation frequency in An. gambiae s.l. pyrethroid resistant following a nationwide distribution of LLINs by the Beninese National Malaria Control Programme. Asian Pacific Journal of Tropical Biomedicine. 2014; 4: 239–243.

100. Rowland, M. "Integrated Vector Management.Outlooks on Pest Management. 2013; Saffron Walden 24.3: 142-143.

101. World Health Organization. Global strategic framework for integrated vector management. 2004; WHO/CDS/CPE/PVC/2004.10: 01-15.

102. Stone C, Chitnis N, Gross K. Environmental influences on mosquito foraging and integrated vector management can delay the evolution of behavioral resistance. Evolutionary applications. 2016; 9(3): 502-517.

103. Beier JC, Keating J, Githure JI, Macdonald MB, Impoinvil DE, Novak RJ. Integrated vector management for malaria control. Malaria journal. 2008; 7(1): S4.

104. Yu SJ. The Toxicology and Biochemistry of Insecticides. CRC Press, Taylor and Francis Group, United States of America. 2008.