INNSPUB

International Journal of Biosciences | IJB |
ISSN: 2220-6655 (Print), 2222-5234 (Online)
http://www.innspub.net
Vol. 16, No. 3, p. 362-370, 2020

REVIEW PAPER OPEN ACCESS

# Mosquitoes and viruses are dual threat to Pakistan: in the era of climate change

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**Key words:** Mosquitoes, Vector, Climate change, Arboviruses.

http://dx.doi.org/10.12692/ijb/16.3.362-370 Article published on March 29, 2020

## Abstract

In the era of climate change, about 80 % of global population is at risk to vector borne viral diseases. The climate changes imparted a significant impact upon the mosquito's ecosystems. Mosquito population highly affected by the temperature variability and water resources. Mosquitoes are insects, feed on blood and transmit pathogenic viruses via biting the particular host. Chikungunya, Dengue fever, Zika fever and West Nile are most prevalent mosquitoes borne viral diseases in Pakistan. Mosquitoes breeding sites are water bodies, discarded tyres harbouring water, water tanks, bottles, cups and ant traps. Pakistan bears the poor living standards therefore, morbidity and mortality rates are much higher with respect to other countries due to these arboviruses diseases. There should be proper sanitation and preventive strategies for elimination of vectors like mosquitoes. This review article aims to highlight the current and future threats of mosquitoes borne viral diseases in Pakistan, in relation to climate change. Proper measures should also be taken to reduce the impact of climate change. If the appropriate steps should not be taken situation become more threatening to Pakistan.

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**Introduction**

Small insects belonging to family culicidae are called mosquitoes. About 3500 mosquito's species have been identified all over the world (www.mosquito.taxonomic –ineventory.info), from which 104 species are recorded from Pakistan and Bangladesh. Most common genera are *Culex* and *Aedes* for the transmission of viruses to human population. Mosquitoes are flying, blood sucking insects and act as a common vector in the transmission of viruses to the host population. Mortality and morbidity rate of viral diseases transmitted through mosquitoes, are very high about 2.5 billion people are at risk to dengue every year. In Pakistan biodiversity of mosquitoes is not that much well known (Ashfaq *et al.*, 2014). Pakistan considered one of the main hotspot for vector mediated diseases. Dengue outbreaks imparted attention toward the study of mosquito population and distribution in Pakistan (Mousson *et al.,* 2005). Different genera of mosquitoes transmit variety of viruses belonging to arboviruses (Badawi *et al.,* 2018).

Arboviruses are transmitted through arthropods especially, mosquito plays a vital role in both 1) human to human transmission through blood tranfusion and also plays a major role in 2) non-human transmission (Ashfaq *et al.,* 2014). The majority of arthropods mediated transmission associated with human diseases achieved by infected arthropods feeding on human. The viruses are transmitted by mosquitoes to reservoir and amplifying hosts that leads to viremia that is enough to infect mosquitoes, vertebrates and human the dead end hosts, become infected potential severe and potential fatal diseases (Huang *et al.,*2019). As shown in Fig 1.

Under certain conditions for example when vectors and are naïve hosts are more abundant, an enzootic cycle limited to specific region becomes epizootic with large number of cases (Huang*et al.,* 2019). Because of requirement viruses replicates in both arthropods and vertebrates hosts this biological transmission creates interaction between vertebrates, viruses and arthropods (Huang *et al.,* 2019). They depend upon water availability (Naeem *et al.,* 2019). Water tanks, water bodies, discarded tyres containing water, bottle and ant traps are the important breeding sites for mosquitoes (Dom, 2013). Pakistan being a subtropical country has greater agricultural land and have open irrigation system which serves as, main breeding sites for mosquitoes.

Factors like vegetation, temperature, water currents and climate changes affect mosquito's population (Ilahi, 2013). Climate change is another horror to the earth population now a day. The increasing temperature and humidity on the earth imparted many impacts to disease patterns. Many infectious diseases became more lethal to human. In our context vector borne diseases, especially mosquitoes mediated diseases exceptionally effected.

The number of mosquito became very abundant due to environmental variations (Fakhruddin *et al.,* 2019). According to the international panel on climate change Pakistan ranked at 5$^{th}$ position in the list of most effected countries by climate change. Therefore, climate change is a serious threat in Pakistan due to its diverse geographical and climatic conditions (Mumtaz *et al.,* 2019). Climate change directly affect the habitat and ecosystems of mosquito. Due to lack of proper diagnostic facilities mostly mosquito borne viral diseases are misdiagnosed. Proper diagnosis is a key factor for the treatment and prognosis of these diseases (Lee *et al.,* 2018). This review article briefly describes the interplay between mosquito borne viral diseases and climate change in Pakistan.

*Chikungunya*

Arbovriuses are considered as the agents of emerging or re-emerging diseases. As classification suggest that arboviral infections are different at different places of the world. The mosquitoes borne arboviruses, chicken gunya, dengue virus, west nile, zika virus, yellow fever virus, Japanese encephalitis and rift valley fever virus have a more regional distribution (Amoa-Bosompem*et al.,* 2020). As shown in Fig 1.

The chickengunya is a viral disease of arbovirus, which is a single- stranded, enveloped RNA virus belongs to family Togaviridae. It is transmitted by *Aedes albopitus*and *Aedes aegypti*species. Based on antigenic properties, CHIKV divided into different sero-complexes (Mohan *et al.,* 2010). Arboviruses have two cycles of transmission urban cycle and sylvatic cycle. Sylvatic cycle concerns with transmission of virus into non-human hosts like monkey or rodents. But urban cycle, mainly concerns with mosquitoes to human's transmission in urban environment (Mayer *et al.,* 2017). These viruses can also be vertically transmitted from mother to fetus and through blood transfusion (Ali *et al.,* 2018).

In Pakistan first case of Chicken gunya was diagnosed on December 2016 (Badar *et al.,* 2019). But this was quite strange that anti- CHIKV antibodies were present in humans and rodents sera since 1980. This disease is specially highlighted in Pakistan due to two key factors 1) misdiagnosed due to its symptoms which are quite similar to dengue fever 2) India has worst outbreak of these diseases. There should be correct diagnosis, for the better treatment and eradication (Badar *et al.,* 2019). Many people in populated areas of Pakistan such as Shah Faisal and Malir in Karachi were suffering from chicken gunya due to poor sanitation conditions and carelessness. Few patients of chicken gunya were also reported in Lahore during 2011 (Mehdi *et al.,* 2019).

The ministry of national health services, regulation and coordination declared 1st time the outbreak of chicken gunya on 26 December, 2016. Based on the finding of WHO concluded an epidemic of chicken gunya in Pakistan (Mehdi *et al.,* 2019). Replication of chicken gunya viruses occur in midgut of mosquitoes. Immediately after the bite of infected mosquitoes, CHKIV recognizes the receptors present on host cells and make sure their entry through endocytosis. Cholesterol level of host cells membranes plays an important role in transmission of viruses into cells. It has been observed that, reduction of infectivity by 65% by limiting the cholesterol level (Ali *et al.,* 2018), Viral replication occurs in both myeloid and lymphoid cells. CHIKV replicates at very high level in the host cells and produce cytopathic effects (Mathew *et al.,* 2017).

*Dengue fever*

Dengue fever is tropical emerging disease of dengue virus, one of the most important vector borne viral disease in Pakistan, caused by single stranded RNA virus belonging to family flaviviridae which has four antigenically different serotypes: DEN-1, DEN-2, DEN-3, and DEN-4 (Yung *et al.,* 2015). Dengue virus is commonly transmitted through a mosquito Aedes aegypti. Which has specific time of bite before the dawn, after the dusk and its secondary vector is *Aedes albopictus* (Chatchen *et al.,* 2017). *Aedes albopictus* was firstly collected from Peshawar in 1934, while *Aedes aegypti* was isolated from Kohat-Hango by Qutubuddin in 1949. They transmit dengue virus by two definite cycles, endemic/ epidemic cycle and sylvatic/ zoonotic cycle (Qutubuddin., 1960) as shown in Fig. 1.

However, the dengue virus made its entry to Pakistan in two definite events, firstly in south areas of Pakistan in 1980s and secondly in north areas of Pakistan in 1993 (Haroon *et al.,* 2019). During 1960-1980 in different provinces of Pakistan sero-surveys were conducted for the checking of neutralizing and Heamaggultination antibodies against dengue virus (Wasim *et al.,* 2014). The prevalence of dengue virus was undocumented in Pakistan before 1994 (Rasheed *et al.,* 2013). Frist case of dengue infection was reported in 1982 from Punjab, Pakistan. In 1994 the first epidemic of dengue fever was reported in Pakistan (Rasheed *et al.,* 2013). A grand survey was conducted in 2000 in five districts of Sindh for the presence of *Aedes aegypti*, survey confirmed the increase in the presence of *aedes agypti*(Wesolowski *et al.,* 2015).

After the break of five years another outbreak of serotype 3 of dengue virus was reported in 2005 in Pakistan. Before 2006, dengue was not common in Pakistan, but after 2006 disease extended his spectrum from south to the north of Pakistan.

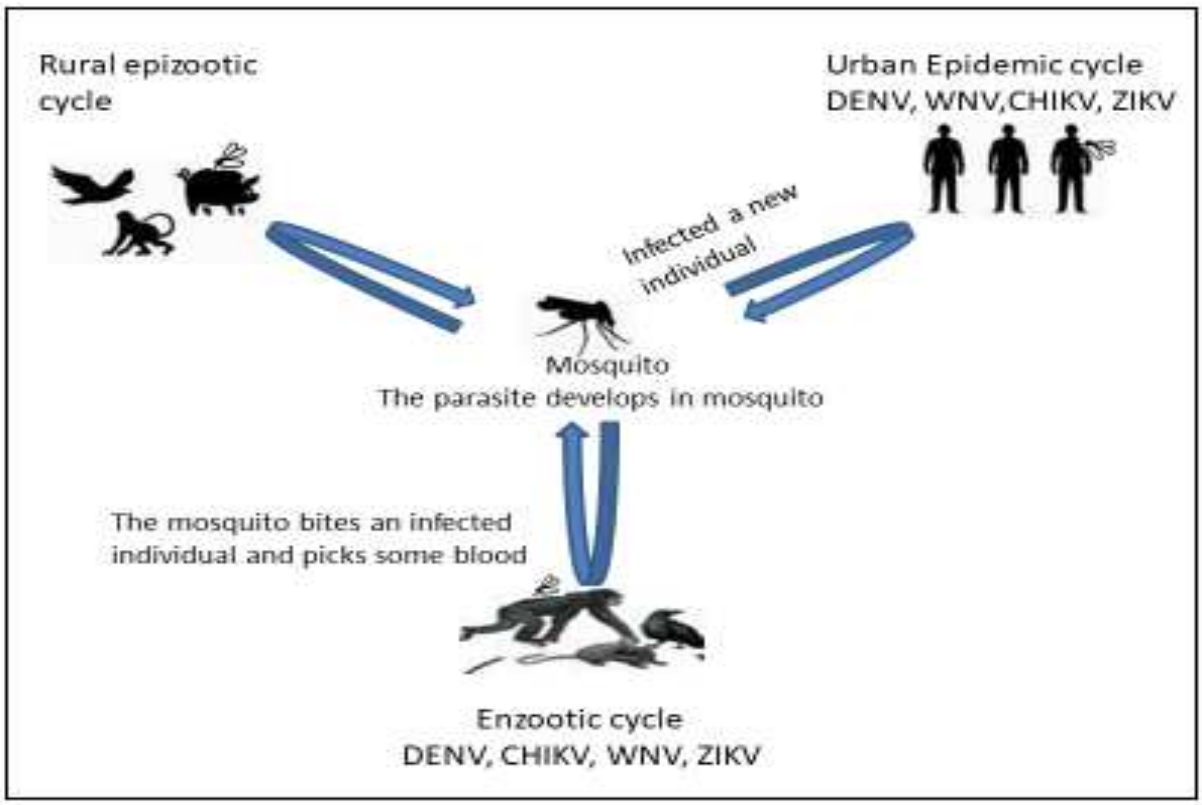


**Fig. 1.** Arboviruses (DENV, West Nile, CHIKV and ZIKA) have two transmission cycles Enzootic transmission cycle and Epizootic transmission cycle. Epizootic transmission cycle is between vector and wild host animals. Enzootic transmission cycle is between vectors and non-wild animals. Humans are dead end host.

In 2013 Pakistan faced the worst outbreak of dengue fever (Wasim *et al.,* 2014). About 50-100 million cases of dengue fever were observed all over the world indicating prevalence of dengue inflated in whole world. After the malaria, dengue fever is ranked at 2nd most lethal disease among mosquitoes borne diseases in human, having mortality rate 1-5%, transmitted only after the bite of infected mosquito into the body through skin (Hasan *et al.,* 2016). The transmission of the dengue viruses is effected by Urbanization, poor sanitation and water availability. There is no effective treatment of dengue fever until now in Pakistan. First vaccine against dengue virus "Denvaxia" developed by Sanofia Pasture is on phase three clinical trial (Wiwanitkit*et al.,* 2010).

*West nile disease*

West Nile Disease is caused by a single stranded, enveloped positive-sense RNA virus belonging to family flavivirus, and transmitted by *Culex*mosquitoes. More than 30 species of *Culex*mosquitoes are present in Pakistan only *Culex tritaeniorhynchus, Culex quinquefasciatus* and *C. quinquefasciatus* are only vector species among all culex mosquito species present in Pakistan. They can spread infections in both human and birds that's why it exhibited enzootic transmission cycle between birds and mosquitoes. Therefore, WNV infections are mainly spread by the birds, by amplifying the viruses as shown in Fig. 1. Accordingly, migratory birds are responsible for the spread of WNV over the long distances and wild birds work as amplifier of domestic WNV strains (Khan *et al.*, 2018). Mild winter condition, droughts, spring season and increased rainfall can significantly increase the epidemics of disease.

Mosquitoes population can increase during these conditions and transmission becomes very high (Caminade *et al.,* 2019). Hence, bird trade, mosquito transportation by shipping, airlines and movements of the people are the key factors which play a significant role in transmission and distribution of WNV. WNV first case was reported in 1982 in

Pakistan but its serological signs examined before it. Epidemiological study that was conducted about twenty years ago determines that 40% humans have antibodies against WNV in Punjab, Pakistan. An outbreak was reported recently in Karachi however investigator cannot detect the viral genome.

The WNV infection can occur through blood transfusions and organ transplantation but the major route of transmission is mosquitos bite. WNV can be Diagnosis by NS1 and IgM ELISA, RT-PCR, Plaque reduction neutralization testing (Khan*et al.*, 2018).

*Zika fever*

Zika fever is a vector borne disease of viruses belonging to flaviviridae, shows different patterns of transmission in different environments. The Zika virus is primarily transmitted through *A. furcifer*, *A. aegypti* and *A. albopictus*, using sylvatic cycle in Aferica involving various species of mosquitoes and non-human primates like rhesus monkey as shown in Fig. 1. Until now, there is no observation recorded in Asia about the sylvatic transmission cycle (Ciota *et al.,* 2017). The transmission depends upon the competence of vectors; low competence means low ability to transmit (Santos *et al.,* 2017). It also bears a human to human transmission cycles such as transmission into fetus from infected pregnant mother.

Because of this borad spectrum activity of transmission, zika virus imparted a serious threat to world. This was firstly identified in rhesus monkey in 1947 but its 1st prominent case in human reported in 1952 (Chouin-Carneiro *et al.,* 2016).

There is no clinical case of zika virus reported in Pakistan until now, but the presence of antibodies against the Zika virus are recorded in serological diagnostic survey's in 1983. Identification of zika virus is quite difficult from other Flaviviruses especially, from dengue virus due to the lack of proper diagnostic facilities in Pakistan. The increasing prevalence of Mosquitoes in Pakistan and south Asia is alarming (Yusuf *et al.,* 2016).

*Climate change interplay with Mosquitoes borne Viral Diseases in Pakistan*

Climate change is defined as any significant and long-term change in the weather conditions on any region of the earth over the significant period of the time. The climate change is about abnormal variation in the environment, by affecting the other factors on the earth (Guisan *et al.*, 2019). Vectors, pathogens and host survive and reproduce within optimal climatic conditions. Climate change emphasis very prominent role to enhance the outbreaks of mosquitoes borne viral diseases in Pakistan such as chicken gunya, dengue fever, west nile and zika fever in relation with weather and mosquitoes. Temperature, precipitation and humidity are the significant factors for the increment of vector borne viral diseases in Pakistan. Precipitation more effects the spread and breading of mosquito's family rather than temperature. If there should be more precipitation, water bodies become more frequently available as the breading sites for mosquitoes and population becomes more prevalent (Caminade *et al.,* 2019).

Due to climate change disease intensity increased by 30 folds during late five decades (Misslin *et al.,* 2016). These parameters of climates change are very important to assess the changes in exposure and susceptibility to dengue virus, zika virus, chicken gunya, west Nile virus and plasmodium in age of climate change. There should be huge fluctuations with regards to future socioeconomic changing scenarios. Many studies are being involved to predict how the infectioness of dengue and vector related characteristics changes. Its intensity of transmission can be calculated by climate projections involves concentration pathways (Rocklöv *et al.,* 2019). During rainy season, droughts and spring transmission rate of viruses and plasmodium becomes very high (Caminade *et al.*, 2019). Aedes can adopted any environmental condition that's why its elimination is very difficult (Misslin *et al.,* 2016).

Unfortunately, there are 216 million cases increased in 2016 with respect to 2015 globally. Some developing countries like Pakistan malaria is rising

with high rate. (Caminade *et al.,* 2019). The temperature has also great influence on breading of mosquitoes. Atmospheric temperature strongly impacts on mosquito's life cycle at the different stages, eggs, Larva and pupa. Warmer temperature shorter the length of mosquito life cycle as compared to cooler one. Therefore, breading rate of mosquitoes becomes very high due to increment in temperature with respects to climate change (Ogden *et al.,* 2019). Now a day Mosquitoes species become resistant to available pesticides with the help of climate change (Bonizzoni *et al.,* 2013).

Because Pakistan is affected on high note with climate change therefore mosquitoes and viruses becomes dual threat to Pakistan. There are many chances of the emergence of many other mosquitoes borne diseases in Pakistan in near future.

*Future threats and recommendation*

Evidences shows that the future climate change if not tackled properly, it impacts on the length of transmission cycle and geographical range of vectors (mosquitoes) (Woodward *et al.,* 2014). Climate and ecosystem change collectively increase the anthropogenic pressure on the environment. These conditions severely affect the biodiversity of mosquitoes. (Keesing *et al.,* 2010).

This is an important question to answer how the anthropogenic conditions impacts on the Vector borne diseases, but it is difficult to answer. This question answer is only hindered by the lack of good quality health and climate change (Caminade *et al.,* 2019). There should be programmatically measure for the climate change impacts on mosquitoes borne viral disease in Pakistan.

There should be proper vector control strategies to check out the horror of climate change and mosquitoes. There are four types of control strategies termed as, Environmental modifications, Use of chemical compounds, Biological control and Genetic control (Bonizzoni *et al.,* 2013). Removal of water from the windows, cups, tyres, sewage places and home so that, we can minimize the breading sites for the mosquitoes. Reduction in population of mosquitoes definitely reduces the transmission of pathogenic viruses (Bonizzoni *et al.,* 2013).

*Vector control strategies*

Chemical control: Mosquitoes can be eliminated by applying pesticides at the different life stages like eggs, larva, pupa, and adult. But the most recent recommendation is, the application of pesticides at their adult stage. This technique shows very fine results for the reduction of mosquitoes (Bonizzoni *et al.,* 2013).

Biological control: It is an emerging control strategy to eliminate mosquito's population. In this technique biological organism and biological products like toxins are used to control the mosquito's population (Bonizzoni *et al.,* 2013).

*Genetic control strategies*

Control of Mosquitoes population or breeding by inducing the mutations in the genome to make competent and sterile. Large scale knowledge has been acquired to understand the mating, fitness and control of quality of mass rearing of genetically modified species (Bonizzoni *et al.,* 2013).

**Conclusion**

Pakistan is a hotspot for the vector borne diseases especially mediated with mosquito, like chicken gunya, dengue fever, west Nile, zika fever and malaria. Due to poor sanitation and lack of preventive strategies their outbreaks increased exceptionally. Thousands of people died due to dengue, chicken gunya and zika during few years in Pakistan. Pakistan bears no diagnostic tools and treatment for these diseases. Now a day these mosquitoes borne diseases become a huge threat to population. There should be immediate actions to control the emerging outbreaks of these diseases.

**Acknowledgement**

I would like to acknowledge Allah almighty who gave me courage to do this project. Secondly, I am very

thankful to my respected supervisor Dr. Maskoor Mohsin Gillani who provide me prestigious guidelines and also remove the technical mistakes of this article.

*Conflict of Interest*

No.

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