The strategies to stop Zika: Insights from Vector ecology

Nitesh Vinodbhai Pandey,
Researcher, Indian Astrobiology Research Centre, Mumbai, India. Address correspondence to Nitesh V. Pandey, niteshpandey@iarc.res.in

Abstract:
The recent emergence of Zika in India has brought the disease again on the international radars. The rapid spread of Zika during its American outbreak is the testimony of its transmission potential. However, this ability of Zika to spread rapidly remains an epidemiological mystery. Based on the insights of vector ecology I have proposed a conceptual framework that answers some of the important questions related to Zika’s transmission potential and the strategies that can be implemented to stop its spread locally as well as globally. The most important insight of this paper is as follows: any disease that causes mild illness in the majority of infected humans would spread rapidly if it is transmitted by Aedes aegypti vector.

Keywords: Zika, Vector ecology, Virulence evolution and Zika control strategies.

Introduction:
Zika virus (ZIKV), a mosquito-borne flavivirus, was first identified in the 1940s in Uganda in Africa [1]. The virus mainly causes a self-limiting disease and therefore was not considered a major threat [2]. However, something very strange happened in Brazil in 2015 that changed the public as well as the scientific perception towards Zika completely [3]. The Doctors in cities in the northeast of Brazil began to see the first startling cases of what today is called congenital Zika syndrome (CZS) – babies born with a range of severe birth defects, including small, misshapen heads (microcephaly) [4]. The doctors suspected and laboratory work soon proved that the damage was caused by a Zika virus infection contracted while the mothers were pregnant [5]. It was estimated that 1.5 million people were infected by Zika in Brazil with over 3,500
cases of microcephaly reported between October 2015 and January 2016 [5,6]. In January 2016, the WHO predicted that the virus was likely to spread throughout most of the Americas by the end of the year and in February 2016, the WHO declared the cluster of microcephaly and Guillain–Barré syndrome cases reported in Brazil – strongly suspected to be associated with the Zika outbreak – a Public health emergency of International Concern [6]. In November 2016, the World Health Organization took away the tag of Global emergency as the cases started declining in the South America [7]. A very recent outbreak in the month of October 2018 in Rajasthan, India has brought Zika back to the radar of International agencies like WHO and CDC [8]. As of now, more than 120 Zika cases have been confirmed in the state of Rajasthan including some pregnant women [8]. I would like to claim that the current Zika cases in India would be the tip of the iceberg. The disease might be prevalent in other states of India too.

One of the most distinctive features of Zika is its ability to spread rapidly. The high transmission potential of Zika could be easily understood based on its outbreak in the Americas from 2014-2016. It is therefore very vital for India and its neighbouring countries to take all the possible measures required controlling the current Zika epidemic of 2018.

The ability of Zika to spread so rapidly is still an unanswered question in epidemiology. In this paper, I am presenting a conceptual framework that intends to solve this epidemiological puzzle around Zika. This conceptual framework is based on the role of vector ecology in transmission dynamics and virulence evolution of vector-borne diseases. As per this conceptual framework, the mobility of the humans would be important in the transmission of diseases which are spread by mosquitoes that either have restricted mobility or very low frequency of contact with the host. The mild variants of the diseases transmitted by such vectors would get more transmitted over the virulent variants. This framework would help us answer the following two most important questions concerning Zika. They are as follows:

1. How does Zika spread so rapidly?

2. How can we control Zika?

**Vector ecology and transmission potential of arboviruses: An integrated conceptual framework**

Zika is transmitted by the *Aedes aegypti* mosquitoes [9]. Vector ecology of these mosquitoes is one of the most crucial components that must be considered to understand the transmission dynamics of Zika. The major ecological variables of the vector that would affect the transmission potential of the disease are **a) The dispersal range of the vector b) Biting time of the vector** (Morning, evening
and night). It is not possible to understand or predict the transmission potential of any vector-borne disease without considering the ecology of vectors. The most important predictions of this conceptual framework are:

1. The mobility of the infected human hosts would play a major role in the transmission of diseases spread by Aedes aegypti vector. 2. The transmission potential of any arbovirus would depend on the inherent virulence of the disease. Diseases that do not affect host mobility like Zika would spread rapidly whereas diseases like Chikungunya that cripple host mobility would have restricted local transmission.

In the following sections, I would elaborate on the role of the two major ecological variables of the Zika vector and their effect on Zika’s transmission potential.

Figure 1: The transmission potential of the arboviruses spread by Aedes aegypti

Diseases like Zika that cause mild symptoms in majority of the cases would spread rapidly. On the other hand diseases that cause debilitating symptoms would have limited transmission potential. Therefore the transmission potential of Zika would be maximum among all the arboviruses.
Dispersal Capacity of *Aedes aegypti*:

The *Aedes aegypti* vector that transmits Zika is very lazy and sessile mosquito [10]. This vector has a mean dispersal rate of 30m and maximum dispersal of 100m [10]. In some cases, it is observed to disperse as less as 10m [10]. These mosquitoes are known to visit maximum three human households in their entire lifetime [11].

In the majority of the cases, Zika-spreading mosquitoes are confined to stay and rest only in one human household [11]. Their density is in fact so low that there is sometimes just one *Aedes aegypti* mosquito for the entire house [11].

The mobility of the human host becomes crucial for the sustenance of the transmission cycle if the vector that spreads the diseases has a limited dispersal capacity. Any arbovirus that causes debilitating symptoms would have limited transmission potential. On the other hand, arboviruses that cause asymptomatic or mild disease in the majority of infected humans would spread very rapidly.

The mobility of the infected humans is not affected much in the case of Zika. The disease causes asymptomatic infection in more than 80% of the cases [12]. The rest of the human subjects who are symptomatic usually have mild symptoms. The mobility of the infected humans is not at all affected in case of Zika. On the other hand, the Chikungunya virus causes severe symptoms like high fever and joint pain in the majority of the cases [13]. The mobility of the reservoir host is negatively affected in case of Chikungunya. Since the mobility of the infected host is important in the transmission of disease spread by *Aedes aegypti*, it is clear that transmission potential of Zika would be much higher than Chikungunya or any other arbovirus for that matter. The mobile humans infected with Zika would go on to infect much more *Aedes aegypti* mosquitoes compared to the immobile and severely sick patients infected with Chikungunya.

The dispersal capacity of the vector also affects the fitness components of the parasites. The mild variants of an arbovirus would have higher Darwinian fitness than their virulent counterparts. The serotypes of the arbovirus that cause self-limiting disease would form the majority of the total infections and such disease would be either asymptomatic or mild in most of the human subjects.

There have been many studies from dengue-endemic region that strongly support this conceptual framework. Independent researchers from different dengue-endemic regions have suggested that patterns of human movement, especially in large urban populations where dengue is endemic, plays a potentially major role in the spread of the virus and its persistence [14].

Stoddard et. al based on their activity space model concluded that dengue is mostly transmitted when people are mobile as well as are engaged in their daily activities [15]. Reiner et.al have shown that it is the friends and relatives of the infected dengue subject who have much higher chances of getting the secondary infection
due to social proximity and not necessarily their neighbours [14]. Padmanabha et. al also concluded that human social behaviour and demography drive patterns of finescale dengue transmission in endemic areas of Colombia [16].

As per one of the predictions of this conceptual framework, the individuals with the mild and asymptomatic disease would form the majority of total infection cases. There have been many recent studies that support the strong role of individuals with mild or asymptomatic disease in the transmission dynamics of dengue. A 2018 study indicates that net infectiousness of people with asymptomatic dengue infections is 80% (median) that of people with apparent or symptomatic infections [17]. Due to their numerical bulk in the infectious reservoir, clinically inapparent infections in total could account for 84% of dengue transmission [17].

Of infections that ultimately result in any level of symptoms, the researchers estimate that 24% of onward transmission results from mosquitoes biting individuals during the pre-symptomatic phase of their infection [17].

Only 1% of dengue transmission is attributable to people with clinically detected infections after they have developed symptoms [17]. The proportional contribution of asymptomatic and mild cases of dengue constitutes the majority of the total transmission [17,18].

Zika as well as Dengue, both cause asymptomatic infections in more than 80% of the cases. In fact a study has confirmed that the epidemiology of Zika share immense similarities with Dengue [19]. However even the symptomatic cases in Zika are mild unlike Dengue. The transmission potential of Zika is even higher than Dengue.

Based on the pieces of evidence presented above it is very clear that the transmission potential of Zika would be highest among the arboviruses transmitted by *Aedes aegypti* because of its tendency to cause mild symptoms in the majority of the cases.

**Biting time of the vector:**

The transmission potential of a disease transmitted by day-biting vector would be higher than the one transmitted by vectors that bite in the night. There have been several studies that have shown that the *Aedes aegypti* mosquitoes bite a lot of visitors or non-residents [14,15,16]. This is obvious because people are much more mobile during the daytime due to their routine activities. It is natural that the mosquitoes would be exposed to humans of different localities as well as the humans would get bitten by *Aedes aegypti* that do not belong to their own home or vicinity. People can get infected due to the mosquito bites they got from a place they had visited recently and not their own home. This could be the home of a friend, relative or even a school and college. However what is more important are the
places called *Aedes aegypti* "hotspots" [20,21]. These are places where *Aedes aegypti* could bite people coming from different regions of the city at the same time, which may lead to rapid transmission of the disease on a wider geographical scale. These infected people would go back home and infect the Aedes mosquito of their own home. These types of hotspots could easily manifest around shops, clinics, salons or any other place where people usually gather. The hotspots are only relevant to the mosquitoes that bite in daytime when humans are most mobile. This does not have implications for the mosquitoes that bite after midnight when people are in deep sleep.

One another very important aspect of *Aedes aegypti* ecology is its ability to cause painless bite [22]. It is usually difficult for any person to recall about the place and time where he was exactly bitten by the mosquito. Aedes mosquitoes are known to bite in a way and on body regions so that the bite goes unnoticed [23].

The asymptomatic and mild cases dominate the total transmission source of dengue. Therefore, asymptomatic and the pre-symptomatic dengue carriers would go on to infect the majority of the mosquitoes of the different house due to their undisturbed schedule and mobility during the daytime [14,17].

It is therefore important for the local government bodies to check for *Aedes aegypti* larvae near or within Shops, offices, Salons and clinics. Vector control activities done mainly around households alone would therefore never solve this problem. The control of the mosquito populations near the hotspot regions are far more important to control the spread of the disease over restricting the same around the human households.

**Implications for pregnant women:**

*Aedes aegypti* is a vector that has a limited mobility and prefers to stay in one household most of the times. The women in urban India are more prone towards *Aedes aegypti* bites when compared to the males living in the same house. This is because the women in India are mostly housewives and therefore most of their time is spent within their respective homes [24]. The pregnant women have an even higher risk of mosquito bites since their mobility gets severely restricted with the progression of pregnancy. The pregnant women are therefore at an inherent risk of getting infected with Zika virus.

A study done to understand the epidemiology of the Chikungunya outbreak in Dhaka, Bangladesh concluded that women were 1.5 times more prone to get bitten by *Aedes aegypti* than the men of their house [13]. The cases of Chikungunya were seen significantly more among women. The disease was also geographically restricted to a region of 300 metres as predicted by the conceptual framework presented in this paper [13].
Pregnant women are at inherent higher risk of getting bitten by *Aedes aegypti* mosquitoes. This is due to the fact that the mosquitoes spend most of their life in one home. Since the mobility of the pregnant women is restricted to their own home, they would be more bitten by *Aedes aegypti*. 
How can we control the Zika virus?: Insights from vector ecology

The destruction of the mosquito larvae within and around the human households would be not enough to control Zika. It would be rather more important to kill the larvae around or near the *Aedes aegypti* hotspots like Shops, Clinics and Salons. These are the regions that could actually accelerate the spread of Zika because individuals getting infected at such hotspots would go back and infect *Aedes* mosquitoes that belong to their home or vicinity. These would help in the sustenance of the transmission cycle and may therefore lead to the very rapid spread of the disease.

Another important measure that must be taken to control Zika is massive surveillance. Since Zika is mostly asymptomatic in majority of the individuals, it would be difficult to take timely measures to the stop the epidemic. It is advisable for the Governments to carry national level surveillance as soon as they detect a Zika outbreak anywhere in the country. Alerting the surrounding states or control measures within the vicinity of reported cases is not going to be enough to stop Zika.
Figure 3: *Aedes aegypti* hotspots

**Aedes Aegypti** Hotspots

1. **Clinics**
2. **Salons**
3. **Offices**

1. Hotspots are places where the *Aedes aegypti* could bite people belonging to different geographical locations. Hotspots could actually accelerate outbreaks of Zika.

2. At the hotspots, *Aedes aegypti* would bite people coming from different localities in the city, or state. The infected individuals would go back and infect the mosquitoes of their own home. This would help in the perpetuation of Zika’s transmission cycle.

3. Destruction of the *Aedes aegypti* larvae around hotspots should be the top priority of any government agency that intends to control Zika.
Conclusions:

I have shown in this paper that the transmission potential of Zika is much more than any other arbovirus transmitted by *Aedes aegypti*. Based on the conceptual framework presented in this paper it is clear that diseases like Zika which cause a mild disease in majority of the infected humans would spread much more rapidly than a disease like Chikungunya that causes debilitating symptoms in majority of the human subjects. The mobility of the infected humans is the most important factor that contributes to Zika transmission. It is therefore important to also consider the role of human movement in controlling the disease rather than working solely on controlling the vectors. It is also important to destroy the *Aedes aegypti* hotspots on priority soon after the detection of Zika cases. The conceptual framework proposed in this paper would be of immense help to local and international bodies that deal in the management and control of emerging infectious diseases.

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References:


