

The Zika Virus: The era of emerging outbreaks

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Introduction:

The dengue virus and its equally infamous cousin, the Zika virus, together infect up to around 400 million people every year. The Zika virus and genomic studies of it have opened fascinating windows into our knowledge of the infectious disease and its relevance in the context of emerging outbreaks.

The Zika virus:

1. The Zika virus is a mosquito-borne flavivirus.
2. Most infections in humans are asymptomatic or with mild symptoms, including fever, rash, and joint pain.
3. The outbreak was characterised by an alarming increase in the number of microcephaly cases in newborns, prompting the World Health Organisation to declare it a public health emergency of international concern in early 2016.
4. From Africa, the Zika virus has spread to Asia, Pacific islands, to the Americas, and beyond. The disease has of late been in the headlines with multiple outbreaks in the last few years in multiple Indian states, including, more recently, Kerala and Karnataka.
5. A significant number of insights have come from the Zika virus's genome.
6. Researchers sequenced the complete genome first in 2007. It has more than 10,000 bases of single-stranded RNA.
7. The genome is also peculiar: it encodes for a large polyprotein, which is further cleaved into capsid, membrane precursor (prM), envelope, and seven non-structural proteins.
8. The diagnosis of a Zika virus infection is mostly through genetic testing.
9. An antibody-based test would be complicated because antibodies produced by the infection can cross-react with those of the dengue (DENV), yellow fever, and West Nile viruses.

Epidemiology and surveillance:

1. The Zika virus has an RNA genome, and thus a very high potential to accumulate mutations. The tools, techniques, and modalities we've developed to track the evolution, genetic epidemiology, and molecular underpinnings of transmission and pathogenesis could be extended to Zika virus outbreaks as well.
2. Genomic studies have suggested that the Zika virus has two lineages: African and Asian.

Zika and microcephaly:

1. The small heads of children born to infected mothers has been one of the more alarming complications of a Zika virus infection.
2. Earlier, based on studies with mice, researchers had suggested that a mutation in one of the

precursor membrane proteins, called prM, of the Zika virus was associated with microcephaly.

3. However, while the large outbreak in South America was caused by lineages of the virus with the specific mutation, only a subset of the relevant pregnancies resulted in microcephaly.
4. The Zika-microcephaly hypothesis also suffered when researchers recorded microcephaly in Thailand following infections of the Asian lineage of the Zika virus that lacked the mutation.
5. Foetal Zika virus infections were associated with heavy viral loads during pregnancy, and the viral load strongly influenced foetal growth.
6. Taken together, the findings underscore the importance of the viral load and DENV infections for the occurrence of microcephaly.

Making it attractive:

1. Zika virus and DENV infections are interesting in their own right.
2. In a recent study in Cell that infections of two viruses in primates encourage specific microbes to grow on the skin by suppressing an antimicrobial peptide, RELM, on the skin.
3. These microbes produce acetophenones, which are volatile molecules that could provide a chemical cue to mosquitoes, attracting them towards the individual and supporting forward transmission of the viruses.
4. The researchers also reported that administering isotretinoin could upregulate RELM and reverse this phenomenon.

Conclusion:

Zika virus and DENV interactions have also been an interesting area of research. A significant body of evidence suggests that a Zika virus infection can significantly increase the risk for severe dengue. As climate change helps drive the spread of vector borne diseases, and global warming brings environmental conditions that favour them to new places, our genomic technologies and such deep insights into the molecular pathogenesis of these viruses will be an important guiding light.

