International Journal of Advanced Community Medicine

E-ISSN: 2616-3594
P-ISSN: 2616-3586
IJACM 2018; 1(2): 33-37
Received: 06-03-2018
Accepted: 07-04-2018

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Zika virus disease

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Abstract
ZIKV (Zika virus) is first major infectious disease related to human birth defects. ZIKV is flavivirus, family Flaviviridae causally associated with Guillain-Barre´ Syndrome, fetal microcephaly and other birth defects. Zika virus diseases discovered about 69 years ago and it remains in relative obscurity, within the span of two years it introduced in Brazil, Latin America and spared rapidly in Asia, USA, Europe and Australia. Detection methods are potentially increases which is positive sign to diagnosis of ZIKV disease and development of vaccine. Sexual transmission of Zika in to male-to-female and male-to-male is documented. There is no conformed vaccination or particular Treatment. In the review, we discussed current epidemiology, virology studies, Diagnosis and Treatment and link between nervous system disorders.

Keywords: Zika virus disease, transmission, ZIKV structure, Guillain-Barre syndrome, human birth defect

Introduction
In 1947, Zika virus found in forest of Uganda via investigation of yellow fever. Meaning of Zika is “over grown” in lugnada language (language of Uganda), in 1952 researcher isolated transmissible agent from monkey’s (Rhesus 766) serum which is later isolated from human victim from tropical region of Nigeria [1-2, 19]. After 60 years from discovery in April 2007, victims reported in Yap Island and Micronesia, recently which observed in Brazil, the Cook Islands, New Caledonia. Serologic evidence of human Zika virus (ZIKV) was reported in Tanzania, Egypt, South Asia including India, Bangladesh, Pakistan, Vietnam, Indonesia, Thailand, Malaysia, the Philippines. In Malaysia ZIKV isolated from *Ae.aegypti mosquitoes.* More, recently outbreaks are documented in outside Africa, Asia and many territories [3-5], according to CDC, the most of zika cases reported in America via travelers who travelling around the infected area either returning or visiting purpose [12]. According to outbreak ZIKV spreading rapidly (Table no. 1).

Virology
Zika virus is a mosquito-borne flavivirus, + ve(S); Flaviviridae (Family) single strand molecule (group IV) having 10794 bases with two non-coding region(5’NCR-3’NCR-ORF-5′-C-prM-E-NS1-NS2A-NS2B-NS3-NS4A-NS4B-NS5-3′) The 3' NCR forms a loop structure and the 5' NCR allows translation via a methylated nucleotide cap or a genome-linked protein [6, 7]. The whole genome is translated in a polyprotein, which is processed co- and post-translationally by host and viral proteases [13] (Figure no 1), replication process of is less similar to other known flavivirus. The virion attaches to the host cell membrane receptors via the envelope protein which induces virion endocytosis, then virus membrane fuses with the endosomal membrane and the ssrna genome of the virus is released into the cytoplasm of the host cell, they translate into polyproteins, non-structural proteins [33]. Replication occurs in cytoplasmic viral factories in dsRNA genome. New virions are transported to the Golgi apparatus and then excreted into the intracellular space where the new virions can infect new host cells [13-16].

Clinical manifestation
Pathology
ZIKV is a mosquito-borne flavivirus transmitted through infected mosquito (Aedes) which also responsible to transmit dengue and chikungunya they aggressive mostly day time biters [19, 28], ZIKV not only spread with mosquito [17, 21, 22].

In non-mosquito transmission associated with fetal microcephaly which spread from mother to fetus during pregnancy(recent case in spain, fatus born with brain damaging disorder-BBC news, New york times) which restrict growth of body parts or possibility to responsible for death, recently reported that zika spared sexually trough semen, [8, 9, 11]. Although the transmission of ZIKV through a blood transfusion has proved by real time PCR and have might possibility to transmit zika from laboratory exposure. ZIKV spreads to lymph nodes, blood circulation and possibly secondary organs, flavivirus responsible for cardiovascular complications.

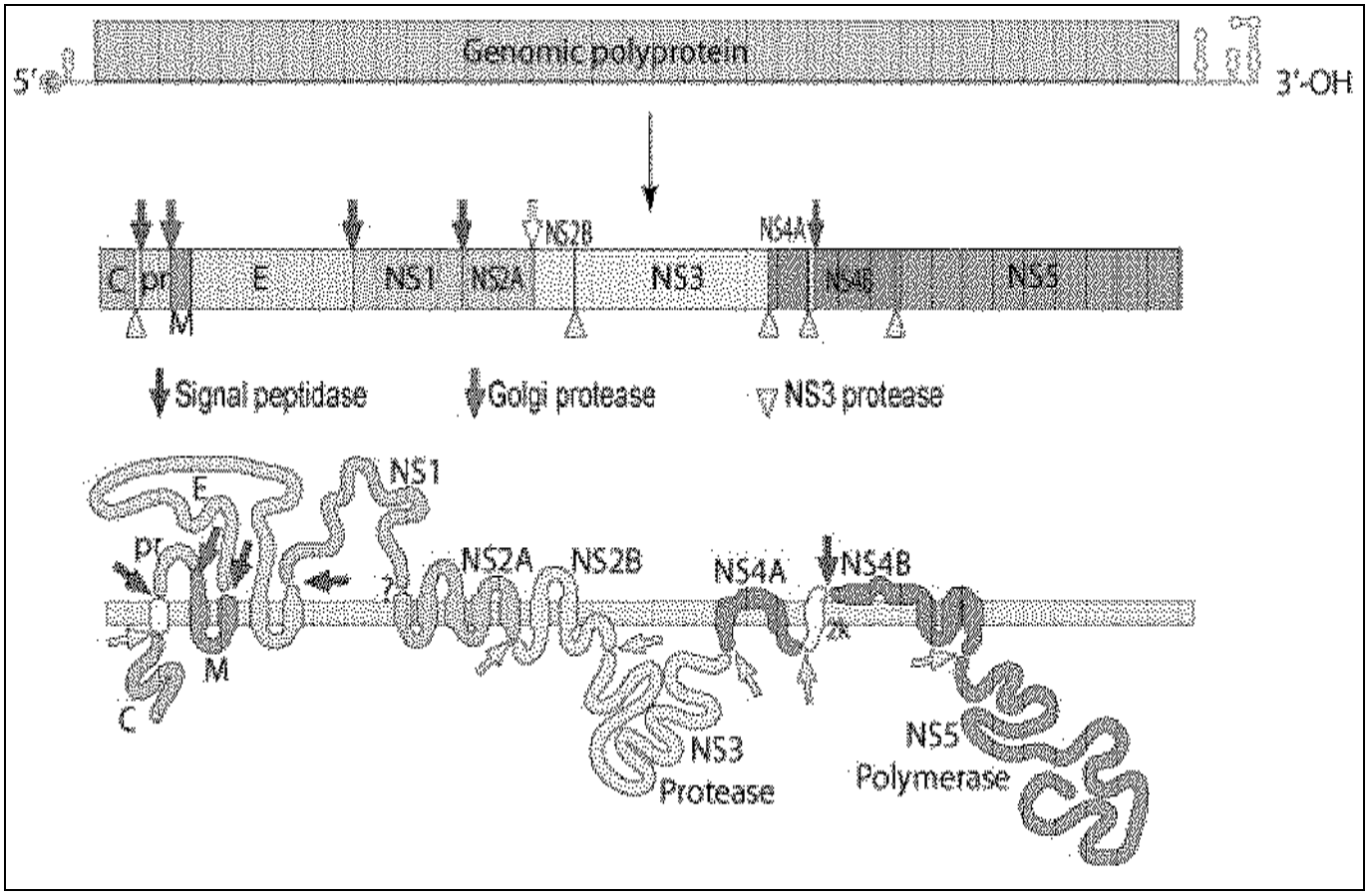

Fig 1: Structure of Flavivirus genome

Symptoms and Care

Death is infrequent, primary symptoms usually fever, Headache, joint pain, Rash, conjunctivitis, rarely nervous system disorder Occurs which can cause temporary paralysis, calcium deposit in the brain. In case of microcephaly symptoms are small head, abnormalities in brain function can causes death in fetus [18-20, 25]. For prevention avoiding mosquito bite by using appropriate insect repellents, if men returning home from affected countries use condoms if their partner is pregnant or might become pregnant. CDC advised pregnant women to travelling in infected territories or countries, who travelling in infected areas should consult with physicians [12, 16, 17].

Diagnosis

Zika virus diagnosis by ZIKV real time PCR [23] and MAC-ELISA (which detect viral ZIKV. ZIKV antibody (IgM) in serum, antibodies find out after 3-4 days after infection but symptoms and tests are closely related with dengue and chickengunya, yellow fever, West Nile viruses. Bo Zhang *et al*. developed a SYBR Green based one-step real-time RT-PCR assay, this assay could detect ZIKV at a titer as low as 1 PFU/mL [32]. ZIKV infection was detected using the anti-4G2 MAb by flow cytometry [15] there is some cross-reactivity with tests for dengue viruses. NS-5 gene (3'coding region) is used for rapid detection of flaviviruses which shows less amino acid identity [26-29]. cDNA from mosquito used in dot-blot membrane digoxigenin diagnosis method. Available primers and probes have been designed on the basis of ZIKV genome sequences. (Table no. 2)

Table 1: Recently important outbreaks

Date	Transmitted Countries	Major Report
22 Feb 2014	Chile	New virus outbreak;40 Suspected cases
25 march 2015	Chile, Brazil	18 cases of unknown illness, reported flushing, pruritus, fever and pain in body
26 march 2015	Chile, Brazil	7 suspect were positive by RT-PCR for ZIKV (369-bp fragment)
15 may 2015	Chile, Brazil	16 cases in Brazil: 8 cases in Bahia State, 8 cases in Rio Grande do Norte State.
30 may 2015	Chile, Brazil	health authorities of the State of Rio de Janeiro have reported the first case(conformation of zikv)
11 June 2015-28 Oct 2015	Chile, Brazil	Above 100 cases are conformed and suspected
28 October 2015	Chile, Brazil Colombia	Cases reported in 5 regions in Colombia (239 cases)
8 November 2015	Guatemala Chile, Brazil Colombia	First case confirmed in Zacapa, Guatemala
18 November 2015	Colombia, Guatemala Chile, Brazil Colombia	reports 393 cases
27 November 2015	Colombia, Guatemala Chile, Brazil Colombia, Mexico	First death reported in Brazil
03 December 2015	Colombia, Guatemala Chile, Brazil Colombia, Mexico, panama	first 3 confirmed cases in Panama, Ustupu island in Guna Yala
11 January 2016	Chile, Brazil, Colombia, Suriname, El Salvador, Mexico, Panama, Venezuela, Honduras, French Guiana, Martinique, Puerto Rico	3,836 cases confirmed in El Salvador
26 January 2016	With above Bolivia, Saint Martin, Haiti, Barbados, U.S. Virgin Islands, Dominican Republic	6 imported cases in Australia reported in 2015; Recent traveler to South America is confirmed case in Virginia, United States
13 February 2016	With above Nicaragua, Jamaica, Curacao, Costa Rica, United States	In Colombia: Cases of the virus total 31,555, among them 5,013 pregnant women.
March 2014, 2016	With above, France, New Zealand, Canada	cases in New Zealand has risen to 61 after reporting 14 new confirmed cases this week; More than 42,700 cases of Zika, including 7653 pregnant women were registered in Colombia, nearly 5,700 new cases in a week
March 14, 2016	With above New Caledonia, Sint Maarten, Laos, Philippines, Italy*, Cuba, Dominica	Colombia reports 55724 Zika cases. Spain has reported five new imported cases in the past week, bringing the country's tally to 43.
July, 2016	With above Bangladesh, Vietnam, Saint Lucia, Belize, Papua New Guinea, Portugal, Republic of auru, Grenada, Peru, Saint Barthélemy, Germany	Germany has confirmed its first case of sexually transmitted Zika virus
Dec, 2016	With above Argentina, Anguilla, Spain, Guinea-Bissau, Sint Eustatius	Honduras reports 25900 suspected cases; Colombia is reporting 8826 confirmed and 89962 suspected cases

GBS (Guillain-Barre´ Syndrome)

GBS is unfamiliar sickness of nervous system, causing muscle weakness, paralysis because its own immune system damages nerve cells. (An autoimmune disorder) according o outbreak in zika it's observed that most of people have GBS who infected with ZIKV. The risk of GBS was estimated to be 0.24 per 1000 Zika infections. Causes factors are still completely not understood, some infectious agent are triggering GBS like DNA Virus(Cytomegalovirus, Epstein Barr virus, Hepatitis B, Herpes Zoster, Herpes Simplex), RNA Virus (HIV, Echo virus, Coxsackie virus, Parainfluenza), Bacteria (Campylobacter jejuni, Legionella, Salmonella typhi, Shigella boydii, Yersinia), No single detection test is present for confirmed diagnosis, sometimes neurological exam finds out loss of sensation. Electro diagnostic testing of the nerves, and spinal fluid analysis. Nerve conduction velocity can me determine disorder. YF-Vax® (Yellow fever Vaccine), Zastavax (Zoster vaccine), Pneumovax (Pneumococcal vaccine), Gardasil (Vaccines for cervical cancer/human papillomavirus vaccine) is used for first line treatment. CDC investigate rises of GBS cases with zika virus infection [5, 12, 25].

Microcephaly

In pregnant women, first trimester Trans placental infection of the NPCs in developing fetus. Zika virus infects Human fetal brain cells. Microcephaly is result of fetal brain disruption sequence, in which, after relatively normal brain development in trimester, collapse of the fetal skull follows the destruction of fetal brain tissue [12-18]. The high rates of microcephaly among infants born to mothers with proven antecedent acute ZIKV infection, provide strong evidence associated with microcephaly to maternal Zika virus infection [27].

Table 2: Primers and probes in ZIKV detection By PCR

Genes	Sequences	ZIKV	Position
M/E	TTGGTCATGATACTGCTGATTGC	ZIKV835	835-857
	CCTTCCACAAAGTCCCTATTGC	ZIKV911c	911-890
	CGGCATACAGCATCAGGTGCATAGGAG	ZIKV860FAM	860-886
pE	CCGCTGCCCAACACAAG	ZIKV1086	1086-1102
	CCACTAACGTTCTTTTGCAGACAT	ZIKV1162c	1162-1139
	AGCCTACCTTGACAAGCAGTCAGACACTCAA	ZIKV1107FAM	1107-1137
E	GCTGGDGCRGACACHGGRACT	ZIKVENVF	1538-1558
	RTCYACYGCCATYTGGRCTG	ZIKVENVR	1902-1883
NS5	CCTTGGATTCTTGAACGAGGA	ZIKVF9027a	9121-9141
	AGAGCTTCATTCTCCAGATCAA	ZIKVR9197ca	9312-9290
NS5	AARTACACATACCARAACAAAGTGGT	5'-3'	9271-9297
	TCCRCTCCCYCTYTGGTCTTG	3'-5'	9352-9373
	CTYAGACCAGCTGAAR	Probe FAM	9304-9320

Treatment

The rapid development of effective ZIKV vaccine is become global health priority. Rafael A. Larocca *et al.* shows that a single immunization of a plasmid DNA vaccine or a purified inactivated virus vaccine gave complete protection against zika in mice model, Vaccines are developed with other flavivirus, GBS, Dengue. There is no confirmed vaccine and Antiviral Drugs against Zika Virus. Primary zika Symptoms treated with getting rest, drinking fluid to prevent dehydration and in chemotherapy such as acetaminophen or paracetamol to reduce fever and pain. Other non-steroidal anti-inflammatory drugs (NSAIDs) and Aspirin, ibuprofen and naproxen, should be avoided until dengue can be ruled out to reduce the risk of increased bleeding [25-26, 33].

Discussion

Zika Virus disease transmitted rapidly in the world, According to documented epidemics ZIKV infection linked with several nervous system disorder and fetal birth defects. There is positive sign for developing diagnosis methods and vaccine development which provide effective therapeutics in future. For gene therapy we can use recombinant adenovirus vector eg. HuAd5. It could be high prevalence of preexisting immunity against HuAd5 in mammalians.

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