INDIAN COUNCIL OF MEDICAL RESEARCH
DIVISION OF EPIDEMIOLOGY & COMMUNICABLE DISEASES

I. Zika Virus preparedness and response

Introduction: ZIKA, a mosquito –borne virus was first identified in monkeys in Zika forest in Uganda in the year 1947. Thereafter, sporadic human cases have been reported in various parts of the world. Outbreaks due to Zika virus have been reported from various countries since 2007. However, in October 2015, Brazil reported association of Microcephaly (an abnormally small head often with consequent brain damage) and later Gulliain Barre Syndrome associated with Zika virus infection. As per information available from WHO, till date, 84 countries, territories or subnational areas have shown evidence of Zika virus transmission. A total of 31 countries and territories have reported Zika associated microcephaly. India's neighbouring countries: Thailand, Singapore, Philippines, Vietnam, Bangladesh etc. have reported Zika transmission.

Mode of transmission & incubation period: Incubation period lasts for a few days (exact duration unknown). Zika virus is transmitted by the bite of infected *Aedes* mosquitoes, which is also the vector of dengue and Chikungunya. Human to human transmission of Zika virus through infected blood and semen is also established. In India, *Aedes* mosquito is widely prevalent.

Clinical picture & Complications: A majority of those infected with Zika virus either remain asymptomatic (up to 80%) or show mild symptoms of fever, rash, conjunctivitis, body ache, joint pains which usually subside between 2-7 days of onset of illness. Based on the available information of previous outbreaks, severe forms of disease requiring hospitalization are uncommon and fatalities are rare.

Treatment: There is no available drug or vaccine effective against Zika virus. Treatment is mainly supportive. Bharat Biotech International Ltd., an Indian company has a Zika vaccine candidate entering shortly into Phase I clinical trials.

Prevention and Control of Zika Virus disease: Vector control is the key to prevention and control of Zika virus infection.

Laboratory Diagnosis: Zika virus can be detected through molecular techniques within the acute phase of illness (3 – 5 days). There is no reliable serological test for diagnosis of Zika. CDC is currently providing Trioplex RT-PCR kits which are FDA approved for emergency use.

Summary of actions taken by ICMR for enhancing preparedness to tackle Zika virus in the country:

i. Capacity building for Zika diagnosis:

ICMR's NIV, Pune has conducted three training programmes wherein they have trained a total of 25 laboratories (including IDSP labs) for Zika virus diagnosis.

The trainings were done from 15th to 19th February 2016, 18th to 22nd October 2016 and 27th – 28th January 2017.

All these labs are routinely testing for Zika virus in dengue and chikungunya negative patients with history of fever or travel. The results are being compiled at NIV, Pune on fortnightly basis.

The list of labs having capacity for testing Zika virus are as follows:

1. King Institute of Preventive Medicine, Chennai, Tamil Nadu
2. NIV Field Unit, Allapuzzha, Kerala
3. Manipal Centre for Virus Research, KMC, Manipal
4. BJ Medical College, Ahmedabad
5. Regional Medical Research Centre, Bhubaneshwar
6. National Institute for Cholera & Enteric Diseases, Kolkata
7. King George Medical University, Lucknow
8. Regional Medical Research Centre, Dibrugarh
9. Regional Medical Research Centre, Jabalpur
10. Jawaharlal Institute of Post Graduate Education & Research, Puducherry
11. Post Graduate Institute of Medical Education & Research, Chandigarh, (VRDL)
12. Desert Medical Research Centre, Jodhpur (ICMR)
13. Amrita Institute of Medical Sciences, Kochi, Kerala
14. Sri Venketswara Institute of Medical Science, Tirupati Andhra Pradesh(VRDL)
15. Gandhi medical College, Secunderabad, Telangana (VRDL)
16. Rajendra Memorial Research Institute of medical Sciences, Agamkuan, Patna(VRDL)
17. All India Institute of Medical Sciences, Bhopal Madhya Pradesh (VRDL)
18. The Tamil Nadu Dr. M. G. R Medical University, Chennai Tamil Nadu,
19. All India Institute of Medical Sciences, Raipur Chhattisgarh
20. All India Institute of Medical Sciences, New Delhi
21. Institute of Preventive Management, Hyderabad
22. Haffkine Institute, Mumbai
23. NIMHANS, Bengaluru
24. Central Research Institute, Kasauli
25. NEIGRIHMS, Shillong

Besides, NIV has also provided primers, SoPs for testing etc to the following laboratories:

1. National centre for Disease Control, Delhi
2. Sher-i-Kashmir Institute of Medical Sciences, Srinagar
3. SMS Medical College, Jaipur

ii. Human surveillance network for Zika virus disease (ZVD) set up by ICMR:

a. Testing of human serum/blood and urine samples for Zika virus is being done by the above 25 trained laboratories. ***Till date, a total of 38400 samples have been tested for Zika virus through this surveillance mechanism.***

b. ICMR has also set up AFI surveillance at BJ Medical College, Ahmedabad wherein samples from febrile patients attending BJMC OPD/IPD (including gynecology OP) referred to VRDL for dengue and chikungunya testing are being aliquoted and stored at the VRDL. These samples are transported to NIV for RTPCR. On an average, the VRDL receives 40-50 samples daily. ***Till date, a total of 953 samples have been tested for Zika virus through this surveillance mechanism.***

c. ANC screening of pregnant women – An aliquot of samples collected from pregnant women attending ANC clinic of BJMC for routine testing (HIV/HBsAg etc) are being collected and stored. These samples are being sent to NIV for ZV serology. ***Till date, a total of 1180 samples have been tested for Zika virus through this surveillance mechanism.***

Till date, a total of 40,533 samples have been tested for Zika virus through the above mechanisms. Samples from three different individuals have been found to be positive for Zika virus.

Details of the three positive cases are as follows:

1. **Details of the first case reported from BJ Medical College, Ahmedabad:**

A 34 year –old female of low socio-economic status, residing at Soneriya Block, Bapunagar, Ahmedabad came to BJ Medical College Hospital for delivery on 9/11/2016. A clinically well baby of 3.7 kg weight was delivered by Caesarean section on the same day. Patient was discharged after one week (on16/11/2016). No history of fever during pregnancy and no history of travel for the past three months. During hospital stay, she developed low grade fever, after delivery. Sample was collected on 14/11/2016, to test for dengue virus. Department of Microbiology at BJMC tested patient's dengue and chikungunya negative serum sample for Zika and found it positive. Patient subsequently had difficulty in wound healing and visited the hospital twice.

Sample from the patient was referred to the Viral Research & Diagnostic Laboratory (VRDL) at BJ Medical College, Ahmedabad for dengue testing. Sample was thereafter found to be positive for Zika virus.

Sample was then referred to NIV, Pune. Further confirmation of etiology by RT-PCR and sequencing has been done. The sample was confirmed as Zika virus positive by Rt-PCR and sequencing at NIV, Pune.

2. **Details of the second case reported from Ahmedabad, Gujarat through active ANC surveillance:**

A total of 111 samples for ANC surveillance were collected from BJ Medical College, Ahmedabad between 6th to 12th January 2017. One sample from a 22 year old pregnant female in 37th week of pregnancy has tested positive.

3. **Details of the third case reported from Ahmedabad, Gujarat through active AFI surveillance:**

A total of 93 blood samples were collected during the Acute Febrile Illness (AFI) surveillance established at BJ Medical College, Ahmedabad, Gujarat. All samples had been collected between 10th to 16th February 2017 and were tested for Zika virus. One sample from a 64-year-old male presenting with febrile illness of 8 days' duration tested negative for dengue infection at BJMC, Ahmedabad. The sample turned out to be positive for Zika virus. This is the first Zika positive case of AFI surveillance at BJMC, Ahmedabad, Gujarat State.

iii. Vector surveillance:

Three ICMR Institutes had initiated limited vector surveillance in different parts of the country since July 2016. List of labs conducting entomological surveillance for Zika virus:

1. Vector Control Research Centre (VCRC), Puducherry,
2. Centre for Research in Medical Entomology (CRME), Madurai,
3. National Institute of Malaria Research (NIMR), Delhi

RESULTS OF XENODIAGNOSIS FOR ZIKA VIRUS:

S. No.	Name of the Institute	Name of the mosquito collection site	No. of Mosquito pools tested	Results
1.	VCRC, Puducherry	i. Kerala state (Thiruvananthapuram, Ernakulam, Malappuram and Kottayam Districts) and ii. Puducherry	987 (11203 *aedes* mosquitoes tested: *aedes aegypti*, *albopictus* and *vittaus*) 74 pools of 610 aedes mosquitoes	Negative for Zika
2.	CRME, Madurai	Tamil Nadu Nilgiris, Kanyaumari, Tirunelveli, Ramanathapuram and Madurai 3 districts	368 pools (8266 *aedes* mosquitoes tested)	Negative for Zika
3.	NIMR, Delhi	Delhi – 130 different localities - South Delhi & West Delhi	374 pools (2825 mosquitoes)	Negative for Zika

Total mosquitoes tested = 22294. Technique used: conventional RT-PCR

Surveillance will soon be expanded to six additional sites.

Results of limited vector surveillance in Gujarat:

A team of ICMR's National Institute of Malaria Research (NIMR), Delhi was sent to Ahmedabad to collect *Aedes* mosquito specimens from the city including the locality from where the first case was reported (in January 2017). Close to 500 mosquito samples were collected from Bapu Nagar locality of Ahmedabad and surrounding regions. All mosquito samples were found negative for Zika.

Future course of action:

- Enhanced human surveillance for Zika virus by:
  - Including private labs in testing.
  - Training more Medical College labs to do testing.
  - Initiating testing in pregnant women and children born with microcephaly.

- ICMR is planning to initiate laboratory testing for microcephaly cases detected in the new born birth screening programme, currently operational in 55 Medical Colleges of the country, through Rashtriya Bal Suraksha Karyakram of the RCH Div. of MoH&FW.

- Vector mosquito surveillance for Zika virus is also being scaled up by training six more labs located in different regions of the country and thus increasing the geographic areas as well as numbers for testing. This will give an indication about mosquito carriage of the virus.

- Review of alternate strategies for vector control in India: ICMR in collaboration with Monash University, Australia is soon initiating work on Wolbachia based vector control for *Aedes* mosquitoes. MoU between ICMR and Monash University has been signed in February 2017.