Maldives

Health Protection Agency

Ministry of Health

Guidelines for Laboratory Surveillance of Zika in Maldives

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Compiled by the

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Contents

1- Background

Zika virus was first discovered in 1947. It is spread by the Aedes mosquito, which also spreads dengue. Symptoms include fever, rash, conjunctivitis, joint pain. Although symptoms are similar to dengue, only 20-25% of people with Zika infection have symptoms and even in these, the symptoms are usually mild, and last from several days to a week.

2- Epidemiology and Virology

The incubation period for Zika is approximately 3-12 days. Although main route of transmission is vector-borne, trans-placental infection has been demonstrated. Sexual transmission has also been documented, but this and other modes of transmission are still being investigated.

Zika virus circulation has been reported in Africa, Asia, Pacific and the Americas, but before 2007, only sporadic cases were reported. Outbreaks were reported from 2007, and the current outbreak in Americas started in May 2015. Between January 2014 and 5 February 2016, a total of 33 countries have reported autochthonous circulation of Zika virus. There is also indirect evidence of local transmission in 6 additional countries.

The main concern with Zika virus at the moment is due to its association with microcephaly in newborns and with neurological syndromes (such as Guillain-Barre' syndrome). However, this has not yet been proven to be causal, and studies are ongoing to establish this.

Zika virus is a Flavivirus. Viraemia is considered to last for about 5 days; however, there is evidence of virus isolation from urine even after 5 days, both detected using RT-PCR. With antibody testing, there is considerable cross-reactivity with antibodies to other Flaviviruses, especially dengue. Therefore, serological tests for Zika infection include plague-neutralization procedures, and ELISA with detection of a four-fold rise in antibodies. Commercially produced kits are not yet available for laboratory diagnosis of Zika.

3- Zika Surveillance in Maldives

With assistance from WHO, Health Protection Agency is working to establish sentinel sites for surveillance Zika virus circulation. Samples from patients who fall within the case definition will be collected and sent to the IGMH lab to test for Zika infection.

3.1 Objectives:

The objectives of this surveillance system are:

- To establish whether Zika infection is being transmitted in Maldives

Further questions such as geographic spread can be answered to a certain extent. In addition, dimensions such as presence of Zika infection in cases of microcephaly or GB syndrome can be tested for if such cases are observed.

3.2 Sites:

Samples are collected from all Atoll/Regional Hospital Laboratory (20 Atolls) whenever a suspected case with Zika symptoms are reported.

In addition to this, samples will also be collected from the following central sites in Male' area;

- Male' (IGMH, ADK Hospital, Senahiya)
- Hulhumale' Hospital

** Note: If a case of microcephaly (according to definition in the Surveillance guideline for Microcephaly- HPA February 2016) or GB syndrome is seen, samples can be sent to test for the presence of Zika infection, even if the cases were detected outside of the these surveillance sites. Contact HPA at (contact number: +9607548221) for sample collection and transport requirements in these cases.*

3.3 Case Definition:

For the purposes of this surveillance, the case definition to be used to recruit patients for sample collection is:

- fever (> 37.8^{o}C) OR maculopapular rash
  with one or more of the following (not explained by any other conditions)
- arthralgia
- myalgia
- non-purulent conjunctivitis
- conjunctival hyperemia
- headache
- fatigue/malaise

In addition the samples taken will be used for diagnostic purposes as well and the result if positive will be shared with the patient.

3.4 Samples:

Samples collected outside IGMH should be sent to IGMH laboratory within 24 hours.

Blood and urine during acute phase (within the first 6 days of symptom onset) and a convalescent sample of both blood and urine (14 days after the first sample) are to be collected. If a patient with history of signs and symptoms of Zika present during the convalescent phase, then only one sample needs to be taken. If the patient presents after convalescent phase then NO sample needs to be taken.

Note: For Pregnant women: In suspected cases, sample should be collected even if the patient presents during or after convalescent phase. Hence, only one sample will be needed. Further guidance is given in Appendix 1- Guidance for Sample Collection, Processing and Shipment.

3.5 Labeling:

At sentinel sites (except IGMH lab), samples will be given a number beginning with the institution code and then the sample number.

e.g. the institution code for Kulhudhuffushi Regional Hospital is KRH. The sample of the first patient should be labeled KRH-001. Both forms and samples should be identified this way.

Each institution will be provided their institution code.

3.6 Procedure:

- Each institution selected should designate an overall focal point and lab focal point for the purpose of sending these samples. The names, designations, email addresses and contact numbers should be shared with IGMH lab and with HPA, (Surveillance or communicable disease division).
- For all those who fall within the case definition criteria, clinicians should fill the investigation form (Appendix 2). The patient name, contact number and permanent address in the page 2 of the form should also be completed. The patient should be given information about the procedure and purpose (refer to page 2 of the form).
- The patient should be directed to the lab, where the details of specimen collection should be filled by laboratory technologist and samples collected according to the guidelines. The lab technician should pack the sample for transport and inform the Focal Point to arrange transportation to IGMH lab within 24 hours. This should be done in contact with IGMH focal point.
- The samples collected should arrive within 24 hours to IGMH lab under transport conditions mentioned in Appendix 1.
- The focal point at each institution should keep records of the patient details and samples collected.
- Forms should be sent along with the samples
- Once IGMH lab received samples, they make a copy of the investigation form. The original form is sent to HPA.

4. Roles and Responsibilities

- Responsibilities of the sentinel focal point:
  - Keeping records according to guidelines
  - Organizing a mechanism within the health facility for convenient sample collection for patients who are coming into provide the sample.
  - Arrange for timely transport of sample to IGMH lab (for sites other than IGMH)
  - Sharing necessary information with HPA and IGMH lab.
  - Making all the necessary arrangements to ensure that the samples taken from the sentinel Lab are transported to the air or sea transport vessel to be transported to Male' or INI Airport.
  - Liaising with (INIA) Border Health Unit and IGMH, for transport of samples from sentinel site to the INI Airport.
  - Maintain a logbook for all the sample transportation, so that the chain of transport can be traced.

- Responsibilities of the clinician
  - Ensuring that all patients that fit the case definition are recruited for sample collection.
  - Fill out the communicable disease forms.
  - Providing information to the patient (see second page of investigation form).
  - Ensuring that all the patient information in the reporting form is completed.

- Responsibilities of the sentinel site lab
  - Completion of the case reporting form.
  - Sample collection.
  - Ensure correct sample identification and labeling.
  - Proper storage and packaging of sample for transport.
  - Liaising with sentinel site focal point for transport of samples to IGMH lab.
  - Maintain a logbook for all the sample transportation, so that the chain of transport can be traced.

- Responsibilities of (INIA) Border Health Unit:
  - Ensure that samples from sentinel sites are transported to Male'.
  - Liaising with the sentinel site and IGMH lab for transport of samples from sentinel site to the INI Airport and for the transport of the samples from the INI Airport to IGMH lab.
  - Maintain a logbook for all the sample transportation, so that the chain of transport can be traced.

- Responsibilities of IGMH lab focal point:
  - Coordinate with sentinel site focal points in receiving samples.
  - Provide information to HPA including originals of the forms.
  - Provide necessary guidance/ training to lab personnel in sentinel sites for the correct collection, storage, transport of samples and documentation.
  - Liaising with the sentinel site and (INIA) Border Health Unit for transport of samples from sentinel site to the INI Airport and for the transport of the samples from the INI Airport to IGMH lab.
  - Maintain a logbook for all the sample transportation, so that the chain of transport can be traced.

- Responsibilities of HPA:
  - Collecting and keeping a database of all patients who have been reported through the communicable disease form.
  - Collecting and keeping a database of all patients whose samples have been taken.
  - Communicate with IGMH about sample transport and results.
  - Arrange all trainings and provide guidance to all sites.
  - Scale up sample collection to include all selected sites based on samples received, the number of dengue cases and completion of trainings.
  - Educate the public and clinicians about the disease.
  - Create mechanism for the transport of the samples from Male' ferry terminal to IGMH lab.
  - Liaising with the sentinel site, (INIA) Border Health Unit and IGMH lab for transport of samples from sentinel site to the INI Airport and for the transport of the samples from the INI Airport to IGMH lab.
  - Maintain a logbook for all the sample transportation, so that the chain of transport can be traced.

5. Annex1-Guidance for the specimen collection processing and shipment

1. Specimen collection and processing

1.1. Serum specimen

1.1.1. To detect Zika virus, the laboratory requires that a serum sample be obtained during the acute phase of the infection (the first 6 days of illness).

1.1.2. All acute specimens will be tested by RT-PCR; virus isolation will be attempted on positive samples.

Type of sample	Interval since the onset of symptoms	Type of analysis
Acute	Until day 6	RT-PCR

1.1.1. For serum sample: collect 4ml of venous blood in a blood collection tube, and allow the blood to clot for 30-60 minutes at room temperature. Repeat this for the next collection tube. In total, 3 tubes (12ml) of blood (red capped blood collection tube) should be collected.

1.1.2. Centrifuge the serum tube at 1800 RPM for continuous 10minutes after the sample is clotted.

1.1.3. Store the tube at 2-8°C (in refrigerator, wet ice, or with ice pack) if the sample can be sent to IGMH within 24hrs.

1.1.4. If there is a delay in sending the sample to IGMH separate the serum to a sterile 2ml micro-centrifuge tube using sterile tips. Store at - 20 ± 10 ^{O}C or with dry ice until arrival at IGMH laboratory.

1.1.5. Samples should be stored in appropriate temperature within 3hrs of sample collection.

1.1.6. While transporting the sample, cold chain should be maintained.

1.2. **Urine specimen**

AT SURVEILLANCE SITES

1.2.1. Collect urine sample (not less than 20ml) in a sterile urine collection cup using the instruction from IGMH below :

1.2.1.1. Thoroughly clean the genital area with soap and water. Dry thoroughly.
1.2.1.2. For females, hold the labia apart while voiding urine. Initiate urination into the toilet, and then bring the container into the stream of urine to collect the middle portion of stream without stopping the flow of urine. Discard the last part of the urine.
1.2.1.3. Urine collection cup should be delivered to IGMH laboratory as soon as possible. For field sites, urine must be transferred to sterile tube and then must be stored at 2-8 ^{O}C, (in refrigerator, wet ice, or with ice pack) until arrival at IGMH laboratory.

Note:

1. **Sample must be stored at 2-8 ^{O}C, in refrigerator, on wet ice or ice pack for no longer than 24 hours.**
2. **For longer than 24 hours, sample must be stored at - 20 ± 10 ^{O}C or dry ice until arrival at IGMH laboratory.**

2. Labeling

At Surveillance Sites

In addition to the standard labeling that is applied to patient lab samples, the Reporting Institution Code (location code + subject code) will be applied on case report form (Investigation of Suspected Zika Infection in Maldives form.

For example: from HDh Kulhudhuffushi the sentinel site code could be KRH and if it is the first sample from there the code should be:

KRH-0001 = HDh Kulhudhuffushi, Subject ID 0001

3. **Report:** Initial lab test results will be reported to authorized personnel of MALDIVES Ministry of Health, Health Protection Agency within 7-10 working days after receiving the specimen at IGMH (Turn-around times for results are subject to change and are dependent on workload).

NOTE: The results of these tests are diagnostic and if positive, it should be informed to the patient and they could be used to direct clinical care.

6. Annex2-Surveillance Form

INVESTIGATION OF SUSPECTED ZIKA INFECTION IN MALDIVES

Health Protection Agency Male',
Republic of Maldives

Reporting Institution : (eg: Kulhudhufushi Regional Hospital)	**CODE** (at IGMH)

A-CASE DEFINITION (Please check the criteria met for this patient)

Suspected case: Patient with
☐rash or ☐elevated body temperature (>37.8° C)_____°C with one or more of the following symptoms (not explained by other medical conditions):

☐ Arthralgias ☐ Myalgias	☐Non-purulent conjunctivitis ☐Conjunctival Hyperemia	☐ Headache ☐ malaise/fatigue	☐ Suspected Dengue ☐ Suspected Chikungunya

Date of onset of symptoms: DD/MM/YYYY	**Date of specimen collection** DD/MM/YYYY
Date of consultation : DD/MM/YYYY	**Type of sample** ☐Serum ☐Urine
Reporting Clinician:	**Phase of Infection**
Clinician Contact Number:	Acute Phase ☐ Convalescent Phase ☐

B-PATIENT DEMOGRAPHICS (tick appropriately)

1- ☐ **Outpatient** ☐ **Inpatient**

2-*Patient Nation ID No: _____ For foreigners include passport number Include copy of ID or Passport	☐ Foreigner (Country of origin): _____ Date Arrived in Maldives: DD/MM/YYYY
3- Age: DOB: DD/MM/YYYY , _____ (Yrs)_____(Mnth)	**4-*Sex:** ☐M (☐F , If pregnant ☐Yes ☐ No)

5- *Patient's Residential Address (pls confirm with patient.)	**6-*Atoll/Island**	**7-Contact number**

8-Recent Travel History (Include countries/atolls/islands visited within 2 weeks prior to symptom onset)

9-Does patient have a known prior history of illness or vaccination with

	Yes	No	Unknown		Yes	No	Unknown	Vaccination
Dengue fever	☐	☐	☐	**Yellow Fever**	☐	☐	☐	☐Yes ☐ No
Chikungunya	☐	☐	☐	**Japanese Encephalitis**	☐	☐	☐	☐Yes ☐ No
West Nile Virus	☐	☐	☐					

10- Clinical Presentation/Additional Symptoms and Information

REPORTING SITE LAB USE **Dispatched by:**_____ **Date:** DD/MM/YYYY	**IGMH LAB USE** **Received by**:_____ **Sample received:** DD/MM/YYYY
HPA SURVEILANCE USE	**IGMH USE**

For further information or inquiries, please contact:
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Sosun Magu, Male'.
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Forms and case definition booklet are available on http://www.hpa.gov.mv , http://www.health.gov.mv