Maldives
Health Protection Agency
Ministry of Health

Maldives Reporting Guidelines for the Surveillance of GuillainBarré syndrome

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Compiled by the
Health Protection Agency
Ministry of Health

Maldives Guidelines for the surveillance of GuillainBarré syndrome

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This guide is based on WHO guidelines and factsheets that are based on currently available data and evidence. This document may be revised and updated in the light of new evidence that may become available.

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Epidemiological background

Guillain-Barré syndrome is a rare acute immune-mediated neuropathic condition in which the peripheral nerves of the body are attacked by the body's own immune system; affecting the nerves controlling muscle strength and nerves transmitting pain, temperature and touch sensations.

Up till the 10th of August 2016, 16 countries and territories worldwide have reported an increased incidence of GBS and/or laboratory confirmation of a Zika virus infection among GBS cases (1) (2). The worldwide incidence of GBS is estimated as 0.8–1.9 (median 1.1) cases per 100 000 people per year among all ages. The annual incidence of GBS increases with age (0.6 per 100 000 per year in children and 2.7 per 100 000 per year in people aged 80 years and over) and the condition is slightly more frequent in males than in females (3).

A 20-fold increase in GBS incidence was observed compared with the previous four years during a

Zika virus outbreak in French Polynesia between October 2013 and April 2014. A study conducted showed a strong association between Zika infection and GBS during the outbreak (3).
Over the past 5 years there have been on average, 2 patients with Guillain-Barré syndrome admitted to IGMH every year. Because of the seriousness of the syndrome, all cases of GBS will be referred to IGMH and so we believe this to be a true baseline value of the average number of GBS cases the in Maldives. We have as yet no GBS cases that can be linked to Zika infection.

It is not always easy or clear to identify the cause of GBS but several causes can trigger it such as, infections like HIV, Dengue, or influenza. Other causes like immunization, surgery or even trauma have been linked with it. Recently there has been evidence to suggest a possible association between zika virus infections and GBS (4).

Proposed Objectives for the surveillance of Guillain Barre' Syndrome

GENERAL OBJECTIVE

- Detect and monitor the prevalence of Zika virus-related GBS in the Maldives.

SPECIFIC OBJECTIVES

- Detect an unusual increase in Zika related GBS
- Monitor the trend in GBS over time
- Disseminate the results in a timely manner
- Provide the basis for undertaking analytical epidemiological studies (case-control and cohorts) that may help to identify and quantify the associated risk factors
- Provide timely information to specialized health care services
- Produce information that may help to characterize the cases

Case definition of GuillainBarré syndrome and Diagnosis

Guillain-Barré syndrome (GBS) is a disorder in which the body's immune system attacks part of the peripheral nervous system. GBS can be triggered by a variety of infections, including dengue and chikungunya viruses. The syndrome can affect the peripheral nerves that control muscle strength as well as those that transmit feelings of pain, temperature and touch. This can result in muscle weakness and loss of sensation in the legs and/or arms. Approximately 25% of GBS patients require intensive care and 3-5% dies even with appropriate supportive care, due to complications related to: paralysis of the muscles that control breathing; cardiac arrest; or blood clots (3).
Most patients with typical GBS present with rapidly progressive bilateral leg weakness with hypo-reflexia or areflexia in the affected limbs. In rare cases, patients can present with Facial, Oculomotor, or Bulbar (i.e. difficulty with swallowing and speaking) weakness, or primary sensory symptoms. GBS is potentially life-threatening, with 20–30% of patients developing respiratory failure requiring ventilation and intensive care support. Up to 70% of patients have some degree

of autonomic instability (i.e. arrhythmias and extremes in blood pressure), with 20% developing serious and potentially fatal autonomic dysfunction. There is a 5% mortality rate, despite optimal care. Approximately 66% of GBS cases are preceded by an infection. Possible triggers are infections including bacteria (e.g. Campylobacter jejuni) and viruses (e.g. Dengue, Chikungunya, Cytomegalovirus, Human immunodeficiency virus (HIV)). GBS may also be triggered by vaccine administration or surgery. GBS has a progressive, monophasic disease course, usually without relapse (3).

Diagnosis

Diagnosis is based on symptoms, findings on neurological examination including diminished or loss of deep-tendon reflexes and lumbar puncture. Other tests, such as blood tests, may be required to identify the cause of trigger of GBS (4).
For the purposes of this surveillance we shall be adhering to the 'Brighton criteria' for diagnosing GBS. The Brighton Collaboration (www.brightoncollaboration.org) is an international collaboration sponsored by the World Health Organization to facilitate the development, evaluation, and dissemination of high quality internationally standardized case definitions for various illnesses, These innovatory 'Brighton criteria' also account for the level of diagnostic certainty based on the presenting findings at clinical and additional examinations, ranging from level 1 (highest level of diagnostic certainty) to level 4 (reported as Guillain-Barre´ syndrome, possibly due to insufficient data for further classification) (5). The weakness limbs and absence or decrease in the deep tendon reflexes in the affected limbs are mandatory features for diagnosis. Temporal association of symptoms, findings from lumbar puncture and neurophysiology testing are supporting characteristics (3).
People with Guillain-Barré syndrome should be treated and monitored; some may need intensive care. Treatment includes supportive care and some immunological therapies (6).
The ICD code for GBS is G61.0, and it is the 2016 ICD-10-CM Diagnosis Code for GuillainBarré syndrome (7).

Signs and Symptoms

Symptoms typically last a few weeks, with most individuals recovering without long-term, severe neurological complications.
The first symptoms of Guillain-Barré syndrome include weakness or tingling sensations. They usually start in the legs, and can spread to the arms and face. For some people, these symptoms can lead to paralysis of the legs, arms, or muscles in the face. In 20-25% of people, the chest muscles are affected, making it hard to breathe.
Severe cases of Guillain-Barré syndrome are rare, but can result in near-total paralysis. These cases are considered life-threatening, and affected individuals are typically treated in intensive-care units.
Most people recover fully from even the most severe cases of Guillain-Barré syndrome, although some continue to experience weakness (5).

Clinical Assessment of GBS

A clinical case of GBS, evaluated by a health care professional with expertise in neurological

examination, should meet the following criteria: bilateral and symmetric weakness of the limbs; decreased or absent deep tendon reflexes in the weak limbs; monophasic illness pattern; interval between the onset and nadir of weakness ranging from 12 hours to 28 days with a subsequent clinical plateau; and absence of an identified alternative cause for the weakness.
A clinical case meets level 3 of diagnostic certainty of Brighton criteria for surveillance and reporting purposes (3).

Cerebrospinal fluid (CSF) examination

Cerebrospinal fluid (CSF) albuminocytological dissociation (CSF protein level above laboratory normative value and CSF total white blood cell count <50 cells/ul) provides supporting evidence for GBS in the appropriate clinical context. Albuminocytological dissociation is present in 50-66% of patients with GBS in the first week after symptom onset and in over 75% of patients in the third week. However, a lumbar puncture performed within one week of symptom onset may show normal results. CSF examination is not needed to make a clinical diagnosis of GBS and should not delay treatment. If there is clinical suspicion of GBS, CSF examination for evaluation of albuminocytological dissociation should be performed as this test provides important supporting data. A repeat CSF examination may be performed one to two weeks after symptom onset if the initial results are normal and the diagnosis of GBS remains uncertain.
CSF examination can be used to arrive at the level 2 of diagnostic certainty of Brighton criteria for surveillance and reporting purposes (3).

Neurophysiology studies

Neurophysiology studies support the diagnosis of GBS and discriminate between GBS subtypes. Abnormalities in neurophysiology testing are most pronounced at least two weeks after the start of weakness, when over 85% of patients have findings consistent with GBS. Nerve conduction studies enable clinicians to categorize GBS into different types such as acute inflammatory demyelinating polyneuropathy, acute motor axonal neuropathy, or acute motor and sensory axonal neuropathy.
Neurophysiology studies are not required to make a clinical diagnosis of GBS and should not delay treatment. Neurophysiology studies provide important supporting data when there is clinical suspicion of GBS. Thus if facilities are available, neurophysiology studies may be done at the time of initial presentation to increase the diagnostic certainty of GBS. Neurophysiology studies may be repeated two weeks after symptom onset if initially normal.
Neurophysiology studies can be used to arrive at the level 1 of diagnostic certainty of Brighton criteria for surveillance and reporting purposes (3).

Laboratory evaluation

Two thirds of GBS cases are preceded by infection.6 There are several potential triggers of GBS including viral (e.g. chikungunya, dengue, HIV) and bacterial (e.g. campylobacter jejuni) infections. Laboratory testing to identify an underlying GBS trigger is not required to make the diagnosis of GBS and should not delay treatment. Laboratory testing to identify a potential trigger should be performed in the context of local epidemiology. Serological testing for HIV infection should be carried out in all patients with GBS.

Laboratory testing to identify Zika virus infection as an infectious trigger of GBS should be done. Testing for GBS should follow the proposed testing algorithm for suspected cases of arbovirus infection as per the above guidance. This includes reverse-transcription polymerase chain reaction (RT-PCR) testing of blood and urine samples and flavivirus IgM testing. Additional testing of CSF samples, including RT-PCR and serological testing (e.g. IgM, IgG, neutralizing antibodies or antibody index) should be considered (3).

SURVEILLANCE PROCESS

It is based on notification to the Health Protection Agency, Surveillance Section (+960 7548221) by the health care facility where the GBS case occurred regarding any event that meets the suspected case definition of GBS for surveillance purposes.

The surveillance system enters the event provisionally, as a suspected case, and triggers a follow-up search for diagnostic tests in order to either include or exclude it as a case related to Zika virus. This process must be done by specialized units, involving clinical assessment (neurological development, genetics, etc.) and complementary diagnostic methods.

Sample collection of blood sample for Zika testing

A blood sample and urine Sample will be collected from patients who are deemed to meet the clinical case criteria of GBS, before they are administered any intravenous immunoglobulin (9).

1. **Specimen collection and processing**

1.1. **Serum specimen**

1.1.1. Collect blood sample (≈3 ml) in a blood collection tube.

1.1.2. After the sample collection, the blood is allowed to clot for 30-60 minutes at room temperature. Blood tubes should then be stored at 2-8 ^{O}C, (in refrigerator, wet ice, or with ice pack) until arrival at IGMH laboratory for centrifugation.

Note: Sample can be stored at 2-8 ^{O}C, in refrigerator, on wet ice or ice pack for no longer than 72 hours before centrifugation.

AT IGMH

1.1.3. Separate serum by centrifugation at 1000-1500 G-Force or Relative Centrifugation Force (RCF) or 1,800 Revolutions per minute (rpm) at 2-8 ^{O}C or room temperature.

Note:

- For the centrifuge with swinging bucket, centrifuge for 10 min.
- For the centrifuge with fixed-angle, centrifuge for 15 min.

1.1.4. After centrifugation, make two aliquots of serum in cryovials and place on ice bath/cold plate at 2-8 ^{O}C. The first aliquot must contain 1 ml. of

serum. The remaining volume of serum will be added to the second aliquot.

1.1.5. After aliquoting, keep serum cryovials in the cryobox(es) and immediately store at - 80 ± 15 ^{O}C until able to ship on dry ice to AFRIMS (see section 2.).

1.2. **Urine specimen**

1.2.1. Collect urine sample 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, 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.**

References

1. **WHO.** Guillain–Barré syndrome. [Online] 2016. http://who.int/mediacentre/factsheets/guillain-barre-syndrome/en/.
2. —. Zika situation report. [Online] August 11, 2016. http://www.who.int/emergencies/zika-virus/situation-report/11-august-2016/en/.
3. —. Identification and management of Guillain-Barré syndrome in the context of Zika virus. [Online] 2016. [Cited: 8 10, 2016.] http://www.who.int/csr/resources/publications/zika/guillain-barre-syndrome/en/.
4. —. Guillain-Barré syndrome (GBS). *World Health Organization.* [Online] 2016. http://www.who.int/mental_health/neurology/guillain-barre-syndrome/en/.
5. —. Guillain-Barré syndrome (GBS). [Online] 2016. http://www.who.int/mental_health/neurology/guillain-barre-syndrome/en/.
6. —. Identification and management of Guillain-Barré. [Online] August 22 , 2016. http://apps.who.int/iris/bitstream/10665/204474/1/WHO_ZIKV_MOC_16.4_eng.pdf.
7. —. [Online] October 2016. [Cited: November http://www.who.int/mediacentre/factsheets/guillain-barre-syndrome/en/, 2016.]
8. **ICD10Data.com.** 2016/17 ICD-10-CM Diagnosis Code G61.0. *ICD10Data.com.* [Online] 2006. http://www.icd10data.com/ICD10CM/Codes/G00-G99/G60-G65/G61-/G61.0.
9. [Online] http://www.gbs-cidp.org/wp-content/uploads/2014/01/2014-Fokke-GBS-Brighton-Brain-2014.pdf.

Annexes

Annex 1: Brighton criteria

	Level of diagnostic certainty			
	1	2	3	4
Bilateral and flaccid weakness of the limbs	+	+	+	+/-
Decreased or absent deep tendon reflexes in weak limbs	+	+	+	+/-
Monophasic illness pattern; and interval between onset and nadir of weakness between 12h and 28 days; and subsequent clinical plateau	+	+	+	+/-
Absence of identified alternative diagnosis for weakness	+	+	+	+/-
Cytoalbuminologic dissociation (i.e. elevation of CSF protein level above laboratory normal value	+	+/-*	-	+/-
CSF total white cell count<50 cells/µl	+	+*	-	+/-
Electrophysiological findings consistent with GBS	+	+	-	+/-
absense of alternative diagnosis for the weakness	+	+	+	+

*If CSF was not collected then the electrophysiological findings must be consistent with GBS in order to categorize as level 2

Annex 2: GuillainBarré syndrome surveillance form

The GBS surveillance form below will be used for surveillance.
All GBS cases must be informed immediately to the Health Protection Agency and the GBS surveillance form filled and sent.
All queries can be directed to disease surveillance hotline +960 7548221 and faxed 3014484

Guillain-Barre Syndrome (GBS) Surveillance Case Report

Health Protection Agency
Ministry of Health
Male', Maldives

CDPH Case ID:

Patient Information (Complete or place ☑ appropriately)

ID Card number:	Date Of Birth: DD / MM / YYYY	Date of Consultation:
Patient Name:		Sex: ☐ Male ☐ Female Age:
Permanent Address:		Pregnant: ☐ Yes (week of gestation): ____ ☐ No
Current Address:		Contact no:

Submitting physician (Required information)

Name:		Date of form completion: DD / MM / YYYY
Email:		Hospital/ Medical Facility:
Contact no:	Fax:	Signature:

Primary care physician/ Physician/ Pediatrician/ Neurologist (Required information)

Name:	Fax:
Contact no:	Signature:

GBS Symptoms (Complete or place ☑ appropriately)

Date of first symptoms: DD / MM / YYYY

(Check all that apply)

- ☐ Acute onset of bilateral and relatively symmetric flaccid weakness/paralysis of the limbs with or without involvement of respiratory orcranial nerve-innervated muscles
- ☐ Decreased or absent deep tendon reflexes at least in affected limbs
- ☐ Electrophysical findings consistent with GBS
- ☐ Presence of cytoalbuminologic dissociation (elevation of CSF protein concentration above the laboratory normal, with CSF WBC <50 cells/mm3)
- ☐ Absence of an alternative diagnosis for weakness

Date of Hospital Admission: DD / MM / YYYY

Is/Was the patient hospitalized: ☐ Yes ☐ No ☐ Unknown

Is/Was the patient in the ICU: ☐ Yes ☐ No ☐ Unknown

If discharged, discharge date: DD / MM / YYYY

Discharge status:
- ☐ Still at admitting hospital
- ☐ Discharged to home
- ☐ Discharge to another healthcare facility
- ☐ Death - Date: DD / MM / YYYY

Imaging Studies (e.g: MRI, CT, etc.)

Results:	Date: DD / MM / YYYY	Contact no:
Reporting Laboratory technician:		Signature:

EMG Study results

Results:	Date: DD / MM / YYYY	Contact no:
Reporting Laboratory technician:		Signature:

CSF 1 Results	F-CSF 2 Results
Date:	Date:
RBC:	RBC:
WBC:	WBC:
%Diff: (neg / lymp / mono / eos)	%Diff: (neg / lymp / mono / eos)
Protein: ____ Glucose: ____	Protein: ____ Glucose: ____

***Campylobacter jejuni* Test Results**

Specimen Type:	
Results:	
Collection Date: DD / MM / YYYY	
Reporting Laboratory technician:	Signature:

Other microbiological studies/results

Data Entry and Quality Checks by HPA

Form Recieved by HPA: DD / MM / YYYY	Data entry: ☐ Yes ☐ No
Name:	Results entry: ☐ Yes ☐ No
Signature	

Past Medical History

Has the patient ever been diagnosed with GBS before?
- ☐ Yes - Date of diagnosis: DD / MM / YYYY
- ☐ No
- ☐ Unknown

Symptoms of possible infection that occurred within 6 weeks prior to onset of GBS-like syndrome? (Check all that apply)

- ☐ Fever (> 38· C) ☐ Diarrhea ☐ Nausea/ Vomiting
- ☐ Upper respiratory (sore throat, rhinorrhea, congestion)
- ☐ Lower respiratory (cough, shortness of breath, wheezing)
- ☐ Rash ☐ Headache ☐ Suspected Dengue
- ☐ Arthalgias ☐ Malaise/fatique ☐ Suspected Chikungunya
- ☐ Myalgias ☐ Conjunctivial Hyperemia
- ☐ Non-purulent conjunctivitis
- ☐ Other – Specify: ____

Other underlying medical conditions?
☐ Yes ☐ No ☐ Unknown Other – Specify: ____

Infection History (Complete or place ☑ appropriately)

Has the patient been diagnosed with any of the conditions below **within 6 weeks** prior to onset of GBS-like syndrome?
☐ Yes ☐ No ☐ Unknown
Other – Specify: ____

☐ Influenza A	Date: DD / MM / YYYY	☐ *Campylobacter*	Date: DD / MM / YYYY
☐ Influenza B	Date: DD / MM / YYYY	☐ CMV	Date: DD / MM / YYYY
☐ H1N1Flu	Date: DD / MM / YYYY	☐ EBV	Date: DD / MM / YYYY
☐ Uknown Influenza	Date: DD / MM / YYYY	☐ Enterovirus	Date: DD / MM / YYYY

Brighton Criteria (Place ☑ appropriately)

Level of diagnostic certainty 1 ☐ 2 ☐ 3 ☐ 4 ☐

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