Guillain-Barré syndrome and other neurological manifestations possibly related to Zika virus infection - Bahia, 2015

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Background

SGB and other neurological manifestations related to Zika virus, Bahia, 2015

June, 12

↑SGB, encephalitis, meningoencephalitis and myelitis

2015

06.10

Situation room
Background

SGB and other neurological manifestations related to Zika virus, Bahia, 2015

- June 12: SGB, encephalitis, meningoencephalitis, and myelitis
- June 19: Meeting with technical areas involved in the state and municipality
- SESAB Technical Note: Hospitals, regional and municipalities, retrospective cases

Situation room

06.10
SGB and other neurological manifestations related to Zika virus, Bahia, 2015

**Background**

- June 12: Increase in SGB, encephalitis, meningoencephalitis, and myelitis
- June 19: Meeting with technical areas involved in the state and municipality
- July 07: SESAB Technical Note for Hospitals, regional and municipalities, retrospective cases
- Panel with experts: Arboviruses and SGB/ MN

**Situation room**
Background

SGB and other neurological manifestations related to Zika virus, Bahia, 2015

June, 12

↑SGB, encephalitis, meningoencephalitis and myelitis

Meeting with technical areas involved in the state and municipality

June, 19

SESAB Technical Note
Hospitals, regional and municipalities, retrospective cases

July, 07

Panel with experts:
Arboviruses and SGB/ MN

August, 13

SESAB PNCD/ SVS/ MS
Video conference

2015

Situation room
Background

SGB and other neurological manifestations related to Zika virus, Bahia, 2015

- **June, 12**: Increase in SGB, encephalitis, meningoencephalitis, and myelitis.
- **June, 19**: Meeting with technical areas involved in the state and municipality.
- **July, 07**: SESAB Technical Note: Hospitals, regional and municipalities, retrospective cases.
- **August, 13**: Panel with experts: Arboviruses and SGB/ MN.
- **August, 17**: Rapid Response Team SVS/ MS.
- **06.10 Situation room**: SESAB PNCD/ SVS/ MS Video conference.

2015
Introduction

In Brazil, in 2015, nine pathogenic arboviruses\(^1\)

Three stand out as sustainable urban circulation: dengue, chikungunya and Zika virus

Relationship between infection by these arboviruses and central and peripheral nervous system involvement\(^2\)

\(^1\) Figueiredo, 2015 \(^2\) Ferreira et al, 2005
Guillain-Barré syndrome\textsuperscript{1,2,3}

Major cause of paralysis in the world, without seasonality described

Annual incidence of 1 to 2 cases / 100,000 inhabitants and peak between 20 and 40 years

\( \uparrow 60\% \) of the patients with GBS presented any previous acute illness

2 to 6 weeks before onset of muscle weakness

Acute or subacute onset, symmetrical ascending muscular weakness, with reduction or absence of reflexes

\textsuperscript{1} Sejvar et al, 2011, \textsuperscript{2} Beneti e Silva, 2015, \textsuperscript{3} Lastra e Heredero, 2015
SGB and other neurological manifestations related to Zika virus, Bahia, 2015

AIM
AIM

SGB and other neurological manifestations related to Zika virus, Bahia, 2015

General

To describe the reported cases of Guillain-Barré syndrome and other neurological manifestations with a history of dengue, chikungunya and Zika infection

Specific

To describe the data by person, time and place

To determine the occurrence of neurological manifestation possibly associated with dengue, chikungunya and Zika virus

To indicate recommendations
Method
Method

Place of study

State of Bahia, population - 15,126,371

Type of study

Descriptive

Study population

Patients hospitalized in the Metropolitan Region of Salvador and Feira de Santana

Study period

01\textsuperscript{th} March to 31\textsuperscript{th} August 2015
Case definitions

Suspected

Patients hospitalized in hospitals in the Metropolitan Region of Salvador and Feira de Santana, who presented:

Neurological manifestation (Guillain-Barré syndrome, encephalitis, meningoencephalitis, myelitis and optic neuropathy) with a history of viral infection up to 60 days before the onset of neurological symptoms, from March to August 2015
Method

SGB and other neurological manifestations related to Zika virus, Bahia, 2015

Case definitions

Probable

Suspected case **without** laboratory confirmation for viral isolation (or by cell culture or molecular biology), but found the following criteria:

**Zika virus** - patient who presented maculopapular rash accompanied by two or more of the following symptoms: fever, polyarthralgia, conjunctival hyperemia, joint edema and pruritus

**Dengue or chikungunya** - clinical epidemiological criteria and / or positive serology (IgM reagent)
Method

Case definitions

Confirmed

Suspected case WITH laboratory confirmation (RT-PCR) for arboviruses (dengue, chikungunya or zika virus):

Zika virus by the RT-PCR technique in cerebrospinal fluid, serum or urine

Dengue and chikungunya by the RT-PCR technique in cerebrospinal fluid or serum
Method

Data source

Epidemiological surveillance worksheet (state and municipal CIEVS\textsuperscript{a})
Revision of medical records in hospitals
Standardized semi-structured questionnaire
Interviews by phone

Laboratory research

Search results of tests in the laboratory environment system
Rescue of collected and stored samples

\textsuperscript{a}CIEVS – Strategic Information Center Of Health Surveillance
**Method**

**Incidence rate**

Annual incidence = No cases SGB / population x 100,000  
Incidence of the outbreak period = Annual incidence / (Outbreak SE/ 52)

**Data processing and analysis**

Epi Info™ 7.1.5.0, QGIS 2.8.2, and Office 2010 Package

**Ethical considerations**

Free and informed consent form (TCLE) - verbal
Results
Results

SGB and other neurological manifestations related to Zika virus, Bahia, 2015

Retrospective search

138* Revised records → 60 Suspects → Losses 3

*In 24 hospitals, a health center And a prompt service unit
Results

SGB and other neurological manifestations related to Zika virus, Bahia, 2015

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N=57

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N=57

51 (89.5%) Likely

6 (10.5%) Inconclusive

Losses 3

*In 24 hospitals, a health center And a prompt service unit
Results

SGB and other neurological manifestations related to Zika virus, Bahia, 2015

**Retrospective search**

138* Revised records → 60 Suspects → Losses 3

N=57

51 (89.5%) Likely

- Zika vírus 30 (58.8%)
- Dengue 13 (25.5%)
- Chikungunya 8 (15.7%)

6 (10.5%) Inconclusive

*In 24 hospitals, a health center And a prompt service unit
Results

SGB and other neurological manifestations related to Zika virus, Bahia, 2015

Distribution of the frequency of GBS cases and other neurological manifestations according to epidemiological week

Number of cases

Incidence in the period of the outbreak:
4.4 cases / 100 thousand inhabitants

N=57

Source: epidemiological research bank
Distribution of the frequency of GBS cases and other neurological manifestations according to neurological manifestations

<table>
<thead>
<tr>
<th>Classification of cases</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>GBS</td>
<td>46</td>
<td>80.7</td>
</tr>
<tr>
<td>Other neurological manifestations</td>
<td>11</td>
<td>19.3</td>
</tr>
<tr>
<td>Myelitis</td>
<td>4</td>
<td>7.0</td>
</tr>
<tr>
<td>Meningoencephalitis</td>
<td>3</td>
<td>5.3</td>
</tr>
<tr>
<td>Others(^\text{a})</td>
<td>4</td>
<td>7.0</td>
</tr>
</tbody>
</table>

\(^\text{a}\)Disseminated acute encephalitis, cervical myelopathy, optic neuritis, unspecified polyneuropathy
Results

SGB and other neurological manifestations related to Zika virus, Bahia, 2015

Distribution of the frequency of GBS cases and other neurological manifestations according to the date of onset of the previous viral infection

Source: SINAN NET / ONLINE and Epidemiological research bank
Results

**Distribution of the frequency of GBS cases and other neurological manifestations according to the date of onset of the previous viral infection and neurological manifestations**

Source: SINAN NET / ONLINE and Epidemiological research bank
Results

SGB and other neurological manifestations related to Zika virus, Bahia, 2015

Distribution of the frequency of GBS cases and other neurological manifestations according to the date of onset of the previous viral infection and neurological manifestations

Source: SINAN NET / ONLINE and Epidemiological research bank
## Results

SGB and other neurological manifestations related to Zika virus, Bahia, 2015

### Distribution of the frequency of GBS cases and other neurological manifestations according to sociodemographic data

<table>
<thead>
<tr>
<th>Sociodemographic</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex, female</strong></td>
<td>77</td>
<td>69.4</td>
</tr>
<tr>
<td><strong>Age Group (years)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤10</td>
<td>2</td>
<td>3.5</td>
</tr>
<tr>
<td>11-20</td>
<td>7</td>
<td>12.3</td>
</tr>
<tr>
<td>21-40</td>
<td>15</td>
<td>26.3</td>
</tr>
<tr>
<td>41-60</td>
<td>20</td>
<td>35.1</td>
</tr>
<tr>
<td>&gt;60</td>
<td>13</td>
<td>22.8</td>
</tr>
</tbody>
</table>

Median (range)

| Age (years) | 44 | 2-83 |
## Distribution of the frequency of GBS cases and other neurological manifestations according to variables of care and hospitalization

<table>
<thead>
<tr>
<th>Variable</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comorbidities, yes</td>
<td>26</td>
<td>45.6</td>
</tr>
<tr>
<td>Hospitalized</td>
<td>57</td>
<td>100.0</td>
</tr>
<tr>
<td>Intensive care unit</td>
<td>20</td>
<td>35.1</td>
</tr>
<tr>
<td>Use of IVIG (N=46)</td>
<td>41</td>
<td>89.1</td>
</tr>
<tr>
<td>Median (range)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interval in days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Home neuro symptoms – Home Use IVIG)</td>
<td>8</td>
<td>6-14</td>
</tr>
</tbody>
</table>
Results

SGB and other neurological manifestations related to Zika virus, Bahia, 2015

Distribution of the frequency of GBS cases and other neurological manifestations according to the evolution of cases

<table>
<thead>
<tr>
<th>Evolution of cases</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>High with improvement</td>
<td>48</td>
<td>84.2</td>
</tr>
<tr>
<td>Transferred to another hospital</td>
<td>6</td>
<td>10.5</td>
</tr>
<tr>
<td>Evolved to death</td>
<td>2</td>
<td>3.5</td>
</tr>
<tr>
<td>Relapse improvement</td>
<td>1</td>
<td>1.8</td>
</tr>
</tbody>
</table>
## Results

SGB and other neurological manifestations related to Zika virus, Bahia, 2015

### Distribution of the frequency of GBS cases and other neurological manifestations according to signs and symptoms of previous acute infection

<table>
<thead>
<tr>
<th>Signals and symptoms</th>
<th>Zika (n=30)</th>
<th>Dengue (n=13)</th>
<th>ChikF (n=8)</th>
<th>Inconclusive (n=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exanthema</td>
<td>30</td>
<td>7</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>Fever</td>
<td>24</td>
<td>11</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Polyarthalgia</td>
<td>22</td>
<td>3</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Itching</td>
<td>23</td>
<td>6</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Myalgia</td>
<td>22</td>
<td>11</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>10</td>
<td>6</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Joint edema</td>
<td>7</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Retroorbital pain</td>
<td>6</td>
<td>2</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Conjunctival hyperemia</td>
<td>3</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Results

SGB and other neurological manifestations related to Zika virus, Bahia, 2015

Distribution of the frequency of GBS cases and other neurological manifestations according to the incidence of Dengue, Chikungunya and Zika

Cumulative incidence BA:
Dengue - 314.4 / 100 thousand population
ChikF - 88.6 / 100 thousand population
Zika - 398.7 / 100 thousand population

Source: SINAN NET / ONLINE and Epidemiological research bank
Limitations
Limitations

SGB and other neurological manifestations related to Zika virus, Bahia, 2015

Difficulty to remember, due to the long period between previous viral infection and the interview

Few laboratory diagnostic results of previous viral infection prevented the classification of arboviruses
Discussion and conclusion
Discussion and conclusion

SGB and other neurological manifestations related to Zika virus, Bahia, 2015

It was identified an outbreak of GBS and other neurological manifestations between SE 18 to 31 and the observed incidence of GBS in the study population was approximately 3 times higher than the expected rate\(^1\).

Interval found between previous viral infection and neurological status, seems to be smaller than the range reported in the literature\(^1,2\).

the introduction and spread of the Zika virus in Bahia, and simultaneous circulation of the dengue virus and chikungunya.

\(^1\) Sejevar et el, 2011; \(^2\) Beneti e Silva, 2015
Discussion and conclusion

There are records of neurological manifestations after infectious processes since the 1960s by the dengue virus and chikungunya.\textsuperscript{1}

There were reports of neurological complications following zika virus since 2007, following outbreaks in Micronesia and French Polynesia.\textsuperscript{1}

Increased number of cases of GBS and other neurological manifestations was identified following the explosion of Zika virus cases in the Bahia State.
Discussion and conclusion

SGB and other neurological manifestations related to Zika virus, Bahia, 2015

The cases with IgM reagent results for dengue, may be false positive. Because the serology for dengue can present a cross-reaction with other flaviviruses\(^1\)

A study carried out in French Polynesia with patients presenting with GBS, most had a history of exanthematic syndrome, 98% had IgM or IgG markers and neutralizing antibodies against Zika virus\(^2\)

\(^{1}\) Marcílio, 2015; \(^{2}\)Cao-Lormeau et al, 2015
Discussion and conclusion
SGB and other neurological manifestations related to Zika virus, Bahia, 2015

The event of neurological manifestations with a history of viral infection may be expected in Brazil, and no longer unusual due to the speed of Zika virus dispersion in the country.

The etiology for this increase in GBS cases and other manifestations even with the hypothesis raised remains in research.
Recommendations
Prospective study aiming at the possibility of collection and confirmation of case for viral diagnosis

Carry out an analytical study to identify and establish the possible relationship and factors associated with the development of GBS and other neurological manifestations and Zika virus infection
Acknowledgments

SGB and other neurological manifestations related to Zika virus, Bahia, 2015

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Municipal Health Secretariat of Salvador / BA
Municipal Health Department of Feira de Santana / BA
Hospitals of public and private network of the state of Bahia
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Método

SGB and other neurological manifestations related to Zika virus, Bahia, 2015

Definição de caso

**Descartado**

Caso suspeito confirmado para outro agente etiológico ou que apresentou outro diagnóstico médico

**Perda**

Ausência do contato telefônico e impossibilidade de realizar entrevista após quatro tentativas em dias e turnos alternados
Distribuição da frequência de casos de manifestações neurológicas com histórico de infecção aguda segundo município de residência
Resultados

Distribuição da frequência de casos SGB e outras manifestações neurológicas segundo incidência de casos de Zika

Vírus Zika + descartados de dengue e chikungunya

*aCasos notificados de vírus Zika + descartados de dengue e chikungunya*
Justificativa

Casos de 'Guillain-Barré' já chegam a 50 na Bahia, indica balanço da Sesab

Dados foram divulgados nesta terça-feira (21) pela Secretaria de Saúde. Do total, 48 apresentavam doenças como dengue, zika ou chikungunya.

Luz vermelha acesa para doença “rara”

Estados do Nordeste começam a adotar estratégias para investigar a misteriosa Síndrome de Guillain-Barré

Síndrome de Guillain-Barré tem 10 casos confirmados no Maranhão


Entre janeiro e julho de 2015, alguns estados da região Nordeste notificaram à Secretaria de Vigilância em Saúde (SVS/MS) a ocorrência de 121 casos de manifestações neurológicas e Síndrome de Guillain-Barré com histórico de doença exantêmática prévia. Investigações estão sendo conduzidas pelo Ministério da Saúde, Secretarias de Saúde de Estados e Municípios da região e outras instituições, como o Instituto Evandro Chagas (IJC/VSMS) e Fundação Oswaldo Cruz (Fiocruz/MS), para subsidiar os Estados e Municípios com orientações amparadas em evidências mais robustas.
Introduction

SGB and other neurological manifestations related to Zika virus, Bahia, 2015

Incidence by Guillain-Barré syndrome (GBS), per month of hospitalization. Bahia and Brazil 2015 *

Incidence in the period:
BRAZIL - 0.49 cases / 100 thousand population
BA - 0.56 cases / 100 thousand population

Incidence GBS\(^1,2\):
0.3 to 0.6 cases / 100 thousand population

Source: SIH/SUS - Datasus

\(^1\)Dourado et al, 2012; \(^2\)Rocha et al, 2004

*Data relating to the period of January to July, 2014 - 2015