Diagnosis and treatment of Guillain-Barré syndrome during the Zika virus epidemic in Brazil: A national survey study

Sonja E. Leonhard 1 | Rodrigo M. Conde 2 | Francisco de Assis Aquino Gondim 3 | Bart C. Jacobs 1,4

1 Department of Neurology, Erasmus University Medical Center, Rotterdam, The Netherlands
2 Ribeirão Preto Medical School, University of São Paulo (FMERP-USP), Ribeirão Preto, São Paulo, Brazil
3 Department of Internal Medicine, Neurology Division, Federal University of Ceará, Fortaleza, Ceará, Brazil
4 Department of Immunology, Erasmus University Medical Center, Rotterdam, the Netherlands

Correspondence
Sonja E. Leonhard, Department of Neurology, Erasmus University Medical Center Rotterdam, Wytemaweg 80, 2015 CN Rotterdam, The Netherlands.
Email: s.leonhard@erasmusmc.nl

Funding information
Erasmus University Medical Center; European Union, Grant/Award Number: 734584

Abstract
The Zika virus (ZIKV) epidemic in Brazil in 2015-2016 was followed by an increase in the incidence of patients with Guillain-Barré syndrome (GBS). With this national survey study, we aimed to gain a better understanding of how neurologists in Brazil are currently diagnosing and treating patients with GBS, and how this increase in incidence has impacted the management of the disease. The questionnaire consisted of 52 questions covering: personal profile of the neurologist, practice of managing GBS during and outside of the ZIKV epidemic, and limitations in managing GBS. All 3264 neurologists that were member of the Brazilian Academy of Neurology at the time of the study were invited to participate. The questionnaire was fully answered by 171 (5%) neurologists. Sixty-one percent of neurologists noticed an increase in patients with GBS during the ZIKV epidemic, and 30% experienced an increase in problems in managing GBS during this time. The most important limitations in the diagnosis and management of GBS included the availability of nerve conduction studies (NCS), beds in the Intensive Care Unit (ICU) and referral to rehabilitation centers. Most neurologists did not use a protocol for treating patients with GBS and the treatment practice varied. Increasing availability of NCS and beds in the ICU and rehabilitation centers, and the implementation of (inter)national guidelines, are critical in supporting Brazilian neurologist in their management of GBS, and are especially important in preparing for future outbreaks.

Keywords
clinical practice, Guillain-Barré syndrome, management, survey, Zika virus

1 INTRODUCTION

Guillain-Barré syndrome (GBS) is the most common acute paralytic neuropathy worldwide, with a global incidence of ~1-2 per 100 000 person-years.1 GBS typically presents as progressive weakness and sensory signs, starting in the distal legs and progressing to the arms and facial muscles.2 Disease progression is rapid and often severe, with ~20% of patients requiring mechanical ventilation due to involvement of respiratory muscles.2 Treatment for GBS generally consists of multidisciplinary supportive medical care and immunotherapy. Both intravenously administered immunoglobulin (IVIg) and plasma exchange are proven effective therapies for GBS.3 GBS is an immune-mediated neuropathy and in most cases presumed to be triggered by specific types of infections.2 Several
pathogens have been associated with GBS in case-control studies. Most recently, infection with Zika virus (ZIKV) was associated with GBS, when incidence peaked during the outbreaks of ZIKV in Latin America in 2015-2016. Brazil was one of the countries most severely affected by the ZIKV epidemic, with ~370,000 cumulative ZIKV cases (suspected or confirmed) reported by the World Health Organization and Ministry of Health between December 2015 and January 2018. The actual incidence is likely to be even higher, as cases may have gone underreported, considering ZIKV usually causes a mild and uncomplicated or subclinical infection. The number of reported cases and the incidence in Brazil was highest in the Northeast, Southeast, and Center-West regions (Figure 1).

It is unknown how neurologists in Brazil are currently managing GBS and if the ZIKV epidemic has affected the diagnosis and treatment of GBS patients. Apart from a protocol mainly directed to guide clinicians in decisions on therapy, there are currently no detailed national Brazilian guidelines for the diagnosis and management of GBS, and at the time of the survey no international guidelines were available. This may complicate the management of the syndrome, especially because clinical presentation and disease progression can differ extensively between patients and specific diagnostic or prognostic markers for GBS are not yet available. Furthermore, it is unknown if neurologists experience limitations in the availability of diagnostic tools, treatment, or care for GBS, and if the increase of GBS patients during the ZIKV epidemic affected such availability.

To gain a better understanding of the current clinical practice in the management of GBS in Brazil and the impact of the ZIKV epidemic, we have conducted a national survey study among Brazilian neurologists. With this survey, we identified limitations in the diagnosis and management of GBS in Brazil, both during and outside of outbreak periods. This information can help in developing strategies to improve the clinical practice of GBS in Brazil, and to prepare for future outbreaks of ZIKV or other pathogens that may trigger GBS.

2 | METHODS

2.1 | Ethical approval

This study was approved by the Ethical Review Board of the Ribeirão Preto Medical School of the University of São Paulo (FMRP-USP) and the National Ethical Research Commission of Brazil (Comissão Nacional de Ética em Pesquisa, CONEP).

2.2 | Questionnaire

The questionnaire was developed by S.E.L., R.M.C., F.d.A.A.G., and B.C.J., and was reviewed for consistency, readability, completeness, and question sequencing by three independent GBS experts. Questions were drafted in English and translated to Brazilian Portuguese by an annotated translation agency. The questionnaire consists of

**FIGURE 1** Number of reported suspected Zika virus cases per state in Brazil, 2016. This figure displays the number of reported suspected ZIKV cases in 2016 per state in Brazil, as published by the Brazilian Ministry of Health in 2017. Not all cases were laboratory confirmed, and other arbovirus infections, were often not excluded. Brazil is divided into 27 states and five regions. The five regions are: North (AC, Acre; AP, Amapá; AM, Amazonas; PA, Pará; RO, Rondônia; RR, Roraima; TO, Tocantins), Northeast (AL, Alagoas; BA, Bahia; CE, Ceará; MA, Maranhão; PB, Paraíba; PE, Pernambuco; PI, Piauí; RN, Rio Grande do Norte; SE, Sergipe), Center-West (GO, Goiás; MT, Mato Grosso; MS, Mato Grosso do Sul; DF, Distrito Federal), Southeast (ES, Espírito Santo; MG, Minas Gerais; RJ, Rio de Janeiro; SP, São Paulo), and South (PR, Paraná; RS, Rio Grande do Sul; SC, Santa Catarina)
52 questions, with 41 multiple choice and 11 open-ended questions, covering several topics, including: personal profile of the neurologist, their practice of managing GBS during and outside of the ZIKV epidemic and limitations they experience in managing GBS. The questionnaire was distributed via an online platform (Limesurvey) that guarantees anonymous and secure data storage and is approved by the Erasmus University Medical Center for the conduction of survey studies.

2.3 Study population

All the neurologists that were member of the Brazilian Academy of Neurology (Academia Brasileira de Neurologia) were approached through the Academy to participate in the survey study. They were contacted via e-mail, containing a link to the online Limesurvey platform. The first invitation was sent in February 2019 and participants had a total of 70 days to answer the questionnaire. Five reminders were sent during that time.

2.4 Analysis

Statistical analysis of multiple-choice questions was done using IBM SPSS Statistics 25 and included descriptive statistics and comparative analyses (Chi square, Fisher’s exact test). Two researchers (S.E.L. and R.M.C) independently grouped open-ended questions into categories. Discrepancies in interpretation were discussed to reach consensus.

3 RESULTS

A total of 3264 neurologists were member of the Brazilian Academy of Neurology at the start of the survey and were invited to participate in the study. Of this group, 254 (8%) answered the questionnaire, and of these responses, 171 (5%) were complete. For the analysis, only fully completed questionnaires were used.

3.1 Profile of the neurologists

The profile of the responding neurologists is described in Table 1. The responders are well-varied regarding age, field of interest, and employment in the private vs public sector. The majority of neurologists work in one hospital (49%), some in two (36%) and a few in three (15%). Most neurologists work in hospitals in the city of São Paulo (11%), Rio de Janeiro (9%), Ribeirão Preto (6%), Belo Horizonte (6%), and Curitiba (5%). Corresponding to this, responders most frequently work in the Southeast region of Brazil (54%), followed by the South (18%), Northeast (17%), Center-Wester (8%) and North (3%) (Figure 2).

3.2 Diagnosis

The clinical practice in diagnosis and treatment of GBS is shown in Table 2. Criteria that were used for diagnosing GBS included the criteria developed by the National Institute of Neurologic Diseases and Stroke (NINDS) (1978, revised in 1990) and by the Brighton Collaboration (2010).10-12 Fifteen percent of the neurologists indicated they used other criteria or no specific criteria.

According to most of the neurologists, cerebrospinal fluid (CSF) testing was (almost) always indicated for diagnosing GBS, but only 4% (almost) always tested CSF in suspected GBS cases. This discrepancy may be explained in part by practical limitations in the opportunity to examine CSF, which were experienced sometimes or frequently by 17% of neurologists (Figure 3). These limitations included the availability of laboratory testing (71%), personnel (33%), equipment (17%), and high costs of the procedure (17%).

Nerve conduction studies (NCS) were available at the hospital of 57% of neurologists. Fifteen percent of the neurologists that indicated NCS were not available at their hospital did not or could not always refer the patient to a dedicated clinic. NCS were frequently or (almost) always indicated in the diagnosis of GBS according to 77% of neurologists, but fewer neurologists (66%) frequently or (almost) always made use of this diagnostic tool (Figure 3). This may be explained by limitations in NCS, that were frequently or (almost) always present in 36% of the responders, and included limited availability of personnel (65%), equipment (57%), high costs of the procedure (24%), and transportation issues.

### Table 1

| Age | Male: Female (ratio) | Years practicing as neurologist | Field of specialization or interest | Number of newly diagnosed GBS cases per year |
|-----|---------------------|------------------------------|-----------------------------------|-----------------------------------------------|
| 40 (34-49) | | 96:75 (1.28) | | | |
| | | 10 (5-20) | General neurology | 103 (64) |
| | | | Neuromuscular disorders | 60 (37) |
| | | | Neuro-immunology | 42 (26) |
| | | | Vascular disorders | 31 (19) |
| | | | Movement disorders | 30 (19) |
| | | | Epilepsy | 27 (17) |
| | | | Neurodegenerative | 26 (16) |
| | | | Pediatric neurology | 12 (7) |
| | | | Neuro-oncology | 5 (3) |
| | | | 0 | 4 (2) |
| | | | 1-5 | 98 (57) |
| | | | 6-10 | 50 (29) |
| | | | 11-20 | 14 (8) |
| | | | >20 | 5 (3) |
| | | | Only public | 49/156 (31) |
| | | | Only private | 64/156 (41) |
| | | | Public and private | 43/156 (28) |

Note: Data are displayed as n/N (%), median (IQR) or n:n (ratio). For questions with multiple answer formats, percentages do not add up to 100.

Abbreviation: GBS, Guillain-Barré syndrome.
Any limitations in CSF and NCS were experienced more often by neurologists working in public hospitals vs those only working in private hospitals, and those working in the Northeast and Center-West vs other regions, although this was only significantly different for CSF examination ($P = .04$, respectively $P < .001$).

### 3.3 Treatment and care

Most of the neurologists did not use a specific protocol to treat GBS patients. Of the 64 neurologists who indicated to use a specific protocol, only seven provided details of this protocol. These protocols included the Protocolo Clínico e Diretrizes Terapêuticas (PCDT), an expert opinion protocol that is approved by the Ministry of Health of Brazil; the American Academy of Neurology (AAN) Guideline on immunotherapy for GBS; and the BMJ Best Practice guideline on GBS.9

When asked what they consider to be the best treatment for GBS, 60% of neurologists answered that IVIg and plasmapheresis are equally effective, followed by 35% who considered IVIg to be the best treatment. However, IVIg was the standard treatment for GBS in the vast majority of responders. According to 48% of neurologists, starting treatment is indicated in all GBS patients, regardless of clinical presentation, severity or progression. When asked what the maximum

### FIGURE 2

Geographic distribution of responding neurologists ($N = 171$). This figure displays the number of responding neurologists per state in Brazil.

![Geographic distribution of responding neurologists](image)

### TABLE 2

Clinical practice of GBS diagnosis and treatment

| Diagnostic criteria used               | 71 (42) |
|---------------------------------------|---------|
| Brighton Collaboration                 | 98 (58) |
| Other or no specific/published criteria | 29 (15) |
| Treatment protocol used               | 64/168 (38) |
| Treatment indication                  |         |
| All GBS patients are treated          | 81/171 (48) |
| Specific treatment indication         |         |
| Rapid disease progression             | 80/90 (89) |
| Inability to walk independently (any distance) | 69/90 (77) |
| Inability to walk independently for 10 m | 13/90 (14) |
| (Imminent) respiratory insufficiency | 76/90 (84) |
| Swallowing dysfunction                | 72/90 (80) |
| Severe autonomic dysfunction          | 72/90 (80) |
| Standard treatment (first line)       |         |
| IVIg                                   | 162 (95) |
| PE                                    | 3 (2)   |
| IVIG and IV corticosteroids (combination) | 4 (2)   |
| IVIg or PE                            | 2 (1)   |
| Alternative treatment (second line)   | 28/54 (52) |

(Continues)
maximum of two times, and 12% had no restrictions in how often they would repeat treatment. Neurologists who indicated to have expertise in neuro-immunology or neuromuscular diseases were more likely to repeat treatment \((P = .02)\), and less likely to switch treatment \((P < .001)\) compared to other neurologists. Treatment practice did not significantly differ between neurologists who had more experience (>5 years) or who saw more \((≥5)\) GBS patients yearly.

Although an ICU was available in the hospital of 96% of neurologists, 55% experienced limitations in transferring GBS patients to the ICU (Figure 4). A limited amount of beds at the ICU was the main problem, indicated by 98% of the responders.

A rehabilitation program was available in the hospital of 77% of the responders. If present, the program included physical therapy (100%), speech therapy (86%), psychosocial support (60%), and occupational therapy (39%). Referral to a rehabilitation unit at discharge was common, although a quarter of neurologists indicated that this was done only sometimes, infrequently, or never or very rarely. Limitations in referring patients to a rehabilitation unit were experienced by the majority of responders, of which 36% experienced this frequently or (almost) always (Figure 4). The most important limitations were a lack of available beds (54%), no rehabilitation center in the region (25%), and limited accessibility of rehabilitation for patients in the public health sector (28%), including delay due to administrative procedures.

Neurologists working in the public sector more frequently experienced any limitations in intensive care \((P = .03)\) and referral to a rehabilitation unit \((P = .03)\) compared to those only working in the private sector. Any limitations in treatment and ICU availability were more frequent in northern states, although this did not statistically differ between regions.

### 3.4 GBS during the ZIKV epidemic

During the ZIKV epidemic in Brazil, 61% of neurologists observed an increase in admissions of patients with GBS in their hospital and 30% of these neurologists experienced an increase in problems in the management of GBS patients. These increased problems included limitations in the opportunity to perform NCS (68%) and CSF examination (27%), availability of beds at the hospital (32%) and the ICU (59%), and availability of treatment (41%). An increase in GBS patients during the ZIKV epidemic was observed most often by neurologists working in the Northeast of Brazil, and an increase in patients or problems in the management were less frequent in the southern regions \((P < .05)\) (Figure 5).

At the time of answering the questionnaire, 59% of neurologists tested for ZIKV in (selected) patients with GBS. Of these neurologists, 74% tested for ZIKV PCR, 73% for ZIKV IgM and only three neurologists indicated to use a plaque-reduction neutralization test.

### 4 DISCUSSION

Neurologists in Brazil often experience limitations in the opportunity to conduct NCS and to refer to the ICU and to rehabilitation centers

---

**TABLE 2** (Continued)

| PE | 12/29 (41) |
| IV corticosteroids | 6/29 (21) |
| Other | 7/29 (24) |
| No response to treatment | 106 (62) |
| Switch to other treatment | 67 (39) |
| Repeat treatment | 13 (8) |
| No additional treatment | 7 (4) |
| Repeat corticosteroids | 7 (4) |

Indication ICU admission: Inability to walk independently (for any distance) 42 (25), Inability to walk independently for ≥10 m 8 (5), (Imminent) respiratory insufficiency 163 (95), Rapid disease progression 142 (83), Swallowing dysfunction 117 (68), Severe autonomic dysfunction 147 (86), Other 3 (2).
when confronted with patients with GBS. Most neurologists saw an increase in GBS patients during the ZIKV epidemic, and one-third of these neurologists also experienced an increase in problems in managing GBS patients during that time. The treatment practice of GBS of neurologists in Brazil is comparable to treatment practice found in other regions, and indicates that international guidelines are necessary, especially to help deciding when to start and when to repeat treatment in patients with GBS.13

Limitations in the diagnosis or treatment of GBS were experienced frequently. Any limitations in NCS were experienced by 60%, in
ICU care by 55%, and in referring patients to a rehabilitation center by 
~30% of neurologists. Especially the lack of availability of sufficient 
intensive care for GBS patients is worrying, as this may directly affect 
morbidity and even mortality of these patients. Limitations were gen-
erally more frequently experienced by neurologists working in the 
Northeast and Center-West of Brazil, which corresponds to a lower 
socioeconomic status in these regions, as reflected by regional contri-
bution to the gross domestic product. Both neurologists working at 
the public and private sector experienced these limitations, but they 
were more frequent in the public health system. So although the 
public health system in Brazil (Sistema Único de Saúde) provides universal 
health coverage for all inhabitants of the country, including access to 
adequate treatment and care for GBS patients, our data indicate that 
in practice, access is not guaranteed and often delayed, and that a lack 
of availability of equipment, treatment, and beds in the ICU and reha-
bilitation centers occur frequently.

During the ZIKV outbreak in Brazil, about 60% of neurologists 
experienced an increased frequency of GBS patients admitted to their 
hospitals, about one-third of whom also experienced an increase in 
problems managing GBS. Increase in patients with GBS was experi-
enced most frequently in the North, Northeast and Center-West of 
Brazil, reflecting the areas that were subject to the highest incidence 
of ZIKV during the outbreak in 2016. Limitations in availability of 
NCS and ICU admission were again the biggest issues. Furthermore, 
only 3% of neurologists indicated to use plaque-reduction neutraliza-
tion test in ZIKV, which is a laboratory test that helps to differentiate 
between a recent ZIKV and dengue virus infection. Due to cross-react-
ivity, ZIKV and dengue virus can be difficult to tell apart based on 
serology, and implementation of this test can be crucial in correctly 
diagnosing patients with ZIKV, especially when PCR results are nega-
tive. Lack of usage of this test suggests that identification of 
ZIKV-related GBS cases may not be optimal.

Most neurologists do not use a specific protocol for treating GBS 
patients, and in some situations the treatment practice varies between 
neurologists or deviates from available evidence from treatment trials. 
First, of the 29 neurologists that use an alternative treatment when 
the preferred treatment (IVIg or plasmapheresis) for GBS is not avail-
able, about 20% use IV corticosteroids, although studies have proven 
that corticosteroids are not effective in treating GBS and may even 
have a negative effect on outcome. Second, about half of neurolo-
gists switch treatment and about a third repeat treatment in patients 
that do not (sufficiently) respond to therapy, although no evidence 
even exists that this is effective. Third, about half of neurologists start 
treatment in all patients with GBS, regardless of their clinical condi-
tion, although effectiveness of plasmapheresis and IVIg has not been suf-
ciently studied in patients still able to walk. This treatment 
practice is also common outside of Brazil, and can likely be explained 
by the lack of evidence and the absence of international guidelines for 
treatment in these situations.

This study has several limitations. First, the percentage of 
responding neurologists was limited, and may be biased toward spe-
cific neurologists, for instance those working in the neuromuscular 
field, in academic hospitals, or in certain regions. Second, the results 
presented reflect the estimates and opinions of neurologists, that may 
deviate from the actual practice.

5 | CONCLUSION

Increasing international migration of humans and vectors pose threats 
of new epidemics of ZIKV or other arbovirus infections, potentially 
related to GBS, resulting eventual upsurge of GBS incidence in the 
near future. Our survey identified several critical limitations in the 
current practice of managing GBS in Brazil and can direct the develop-
ment of strategies to improve this. Most importantly, the lack of avail-
ability of NCS, intensive care management and rehabilitation of GBS 
should guide redistribution of available funding from the Brazilian 
government or (inter)national nonprofit organizations. Furthermore,
treatment practice of GBS is variable and few neurologists use guidelines in treating patients with GBS. Increasing the visibility of the existing national expert opinion protocol for the management of GBS (PCDT), or implementation of a recently published expert-based international guideline for the management of GBS may help to provide such guidance.9,21

ACKNOWLEDGEMENTS
This study is supported by ZikaPLAN, a global research consortium funded by the European Union within the Horizon2020 program (grant agreement number: 734584). We gratefully thank the Brazilian Academy of Neurology for supporting the survey and the Brazilian neurologists for their participation. We thank Dr Merel Broers, Dr Melissa R. Mandarakas and Dr Alex Y. Doets (Erasmus University Medical Center, Rotterdam, The Netherlands), Dr Mario Emilio Dourado (Universidade Federal do Rio Grande do Norte, Natal, Brazil), and Dr Maria Lúcia Brito Ferreira (Hospital da Restauração, Recife, Pernambuco, Brazil) for their feedback on the draft version of the questionnaire. We are also thankful for the support of prof. Dr Amilton A. Barreira in constructing the preliminary version of the questionnaire and establishing contact with the Brazilian Academy of Neurology. Due to his untimely death he could unfortunately not further contribute to this study.

CONFLICT OF INTEREST
S.E.L. declares no conflict of interest. R.M.C. declares no conflict of interest. F.d.A.A.G. declares that he received honoraria from Baxter and CSL Behring to be speaker in IVIg treatment. B.C.J. has received funding from Annexon Biosciences, Baxter, CSL Behring, Hansa Biopharma and Grifols.

AUTHOR CONTRIBUTIONS
S.E.L. and B.C.J. conceptualized the study. All authors designed the questionnaire. S.E.L. and R.M.C. structured the database for analysis and S.E.L. performed all the analyses. S.E.L. wrote the first draft of the manuscript. All authors contributed to the discussion of article content and edited the manuscript before submission.

ORCID
Sonja E. Leonhard https://orcid.org/0000-0003-4832-6926

REFERENCES
1. Sejvar JJ, Baughman AL, Wise M, Morgan OW. Population incidence of Guillain-Barré syndrome: a systematic review and meta-analysis. Neuroepidemiology. 2011;36:123-133.
2. Willison HJ, Jacobs BC, van Doorn PA. Guillain-Barré syndrome. Lancet. 2016;388:717-727.
3. Hughes RA, Swan AV, Raphael JC, Annane D, van Koningsveld R, van Doorn PA. Immunotherapy for Guillain-Barré syndrome: a systematic review. Brain. 2007;130:2245-2257.
4. Jacobs BC, Rothbarth PH, van der Meche FG, et al. The spectrum of antecedent infections in Guillain-Barré syndrome: a case-control study. Neurology. 1998;51:1110-1115.
5. World Health Organization. Zika situation report February 5, 2016. World Health Organization. 2016: https://www.who.int/emergencies/zika-virus/situation-report/5-february-2016/en/.
6. Parra B, Lizarazo J, Jimenez-Arango JA, et al. Guillain-Barré syndrome associated with Zika virus infection in Colombia. N Engl J Med. 2016;375:1513-1523.
7. Pan American Health Organization. Zika suspected and confirmed cases reported by countries and territories in the Americas Cumulative cases. Washington, DC: Pan American Health Organization; 2015–2017. Updated as of January 4, 2018.
8. Pan American Health Organization. Zika · Epidemiological Report Brazil. Washington, DC: PAHO; 2017.
9. Protocolos Clinicos e Diretrizes Terapêuticas - PCDT Sindrome de Guillain-Barré. 2015:http://www.saude.gov.br/protocolos-e-diretrizes.
10. Sejvar JJ, Kohl KS, Gidudu J, et al. Guillain-Barré syndrome and fisher syndrome: case definitions and guidelines for collection, analysis, and presentation of immunization safety data. Vaccine. 2011;29:599-612.
11. Asbury AK, Arnason BGW, Karp HR, McFarlin DE. Criteria for diagnosis of Guillain-Barré syndrome. Ann Neurol. 1978;3:565-566.
12. Asbury AK, Comblath DR. Assessment of current diagnostic criteria for Guillain-Barré syndrome. Ann Neurol. 1990;27(Suppl):S21-S24.
13. Verboon C, Doets AY, Galassi G, et al. Current treatment practice of Guillain-Barre syndrome. Neurology. 2019;93:e59-e76.
14. Organisation for economic co-operation and development (OECD). 2019:https://data.oecd.org/brazil.htm.
15. Secretaría de Vigilancia en Salud Ministro de Salud. Boletín Epidemiológico. Monitoramiento de los casos de dengue, febre de chikungunya e febre pelo virus Zika até a Semana Epidemiológica 52, 2016 [Epidemiologic Bulletin, Monitoring of dengue, chikungunya and Zika virus cases until epidemiologic week 52, 2016]. Boletin Epidemiológico. 2017;48(3). http://www.saude.gov.br/boletins-epidemiologicos.
16. Abushouk AI, Negida A, Ahmed H. An updated review of Zika virus. J Clin Virol. 2016;84:53-58.
17. Waggoner JJ, Pinsky BA. Zika virus: diagnostics for an emerging pandemic threat. J Clin Microbiol. 2016;54:860-867.
18. Chevret S. Plasma exchange for Guillain-Barré syndrome. Cochrane Database Syst Rev. 2017:2:CD001798.
19. Hughes RA, Swan AV, van Doorn PA. Intravenous immunoglobulin for Guillain-Barré syndrome. Cochrane Database Syst Rev. 2014;7:CD002063.
20. Díaz-Soto S, Chavez K, Chaca A, Alanya J, Tirado-Hurtado I. Outbreak of Guillain-Barré syndrome in Peru. eNeurologicalSci. 2019;14:89-90.
21. Leonhard SE, Mandarakas MR, FAA G, et al. Diagnosis and Management of Guillain-Barré Syndrome in Ten Steps. Nat Rev Neurol; 2019.