Large Outbreak of Guillain-Barré Syndrome, Peru, 2019

César V. Munayco, Ronnie G. Gavilán, Gladys Ramírez, Manuel Loayza, Maria L. Miraval, Erin Whitehouse, Radhika Gharpure, Jesus Soares, Hans Vasquez Soploupo, James Sejvar

Author affiliations: Centro Nacional de Epidemiología Prevención y Control de Enfermedades, Lima, Peru (C.V. Munayco, G. Ramírez, M. Loayza); Instituto Nacional de Salud, Lima (R.G. Gavilán, M.L. Miraval, H.V. Soploupo); Centers for Disease Control and Prevention, Atlanta, Georgia, USA (E. Whitehouse, R. Gharpure, J. Soares, J. Sejvar)

DOI: https://doi.org/10.3201/eid2611.200127

Outbreaks of Guillain-Barré syndrome (GBS) are uncommon. In May 2019, national surveillance in Peru detected an increase in GBS cases in excess of the expected incidence of 1.2 cases/100,000 population. Several clinical and epidemiologic findings call into question the suggested association between this GBS outbreak and Campylobacter.

Guillain-Barré syndrome (GBS) is the most common form of acute flaccid paralysis worldwide (1). It is characterized by motor weakness, areflexia, sensory abnormalities, and cytoalbuminologic dissociation in cerebrospinal fluid (2). An upper respiratory or gastrointestinal illness typically precedes GBS (3). Campylobacter jejuni infection is the most frequently identified precipitant of GBS and usually is associated with the acute motor axonal neuropathy form of GBS (4).

During the week of May 26, 2019, the Peruvian Ministry of Health surveillance system detected several cases of suspected GBS that exceeded the expected incidence of 1.2 cases/100,000 persons/year (i.e., 29 cases/year) (1). Since 2016, hospitals in Peru have reported suspected GBS cases to a passive surveillance system (https://www.dge.gob.pe/portal/index.php?option=com_content&view=article&id=653). In early May 2019, when the system was modified to an active surveillance system because of increasing incidence, the National Center of Epidemiology, Prevention, and Disease Control solicited cases. Examining physicians classified cases in accordance with the Brighton Collaboration case definition for GBS (5). The Instituto Nacional de Salud tested serum, urine, nasal swab samples, and feces for infectious pathogens using molecular panels for multipathogen detection (bioMérieux, https://www.biomerieux-diagnostica.com) and conventional microbiology assays.

During May 20–July 27, 2019, we identified 683 suspected or confirmed GBS cases in Peru. The largest outbreaks of GBS have involved ≈30–50 cases, except for large GBS outbreaks associated with Zika virus infection; thus, this outbreak was extremely unusual because of its size. Of the cases, 32 (6.9%) were Brighton level 1, 188 (27.5%) were Brighton level 2, and 463 (67.7%) were Brighton level 3. We classified Brighton levels 1 and 2 cases as confirmed, and Brighton level 3 cases as suspected (Figure; Appendix Figures 1, 2, https://wwwnc.cdc.gov/EID/article/26/11/20-0127-App1.pdf). Nine of Peru’s 24 departments reported GBS cases, which resulted in an annualized incidence of 30.9 cases/100,000 persons/year (Table).

Of the 683 GBS patients, 287 (42.0%) had descending muscle weakness and 446 (65.3%) had ascending muscle weakness. Of 530 patients for whom data on
antecedent illness were complete in the 4 weeks before neurologic symptom onset, 219 (41.3%) reported respiratory and gastrointestinal infections, 195 (36.8%) reported only a respiratory infection, 3 (0.6%) reported only a gastrointestinal infection, and 113 (21.3%) did not report any infection. Of 426 patients for whom hospitalization data were available, 64 (15.0%) required mechanical ventilation. Of 147 patients who had an electrodiagnostic exam, 100 (68.0%) had acute motor axonal neuropathy.

Clinical samples received by Instituto Nacional de Salud were as follows: serum (622 samples), urine (191), cerebrospinal fluid (230), nasal and pharyngeal swab samples (394), and feces (362) (Appendix Tables 1–3). We detected *Campylobacter* spp. in 19 (5.2%) fecal samples. Fecal cultures yielded 8 isolates confirmed as *C. jejuni* biotype I by Gram stain (6). Isolates were highly related by core-genome multilocus sequence typing and were sequence type 2993, Penner serotype HS:41.

This GBS outbreak was unusual because of the large number of cases. The incidence rate was nearly 25 times higher than expected (7) and higher than previously described GBS outbreaks. The rapid increase in numbers, followed by an equally precipitous decrease, might suggest a point-source exposure. The outbreak affected many geographically disparate

| Characteristic | No. cases | Population | Cases/100,000 population |
|---------------|-----------|------------|--------------------------|
| Sex           |           |            |                          |
| M             | 401       | 10,416,496 | 3.85                     |
| F             | 282       | 10,882,518 | 2.59                     |
| Age, y        |           |            |                          |
| 0–11          | 48        | 4,321,980  | 1.11                     |
| 12–17         | 45        | 2,223,271  | 2.02                     |
| 18–29         | 118       | 4,498,823  | 2.62                     |
| 30–59         | 333       | 7,870,813  | 4.23                     |
| >60           | 139       | 2,384,127  | 5.83                     |
| Area          |           |            |                          |
| Junín         | 132       | 1,389,850  | 9.50                     |
| Piura         | 115       | 1,901,896  | 6.05                     |
| Cajamarca     | 53        | 1,543,104  | 3.43                     |
| La Libertad   | 57        | 1,956,389  | 2.91                     |
| Lambayeque    | 31        | 1,300,720  | 2.38                     |
| Lima          | 247       | 10,458,367 | 2.36                     |
| Callao        | 25        | 1,067,815  | 2.34                     |
| Huancavelica  | 10        | 509,117    | 1.96                     |
| Ancash        | 13        | 1,171,756  | 1.11                     |
| Total         | 683       | 21,299,014 | 3.21                     |
| Peru, total   | 709       | 32,526,084 | 2.18                     |

Figure. Cases of Guillain-Barré syndrome classified by Brighton Collaboration criteria (5) and date of illness onset, Peru, May–July 2019.

Table. General characteristics of persons with Guillain-Barré syndrome, Peru, 2019.
regions, including some that differed substantially in geoclimatic properties.

General demographic features, such as slight male predominance and greater incidence with increased age, are typical for GBS (7). However, in many patients, a descending, rather than the more common ascending, paralysis developed (8). The clinical significance of this observation is unclear. Electrophysiologically, most cases appeared to have the acute motor axonal neuropathy phenotype of GBS, which has been closely associated with antecedent C. jejuni infection (9).

PCR and culture detected the C. jejuni outbreak reported here. Genetic analysis confirmed the clonality of these isolates recovered from affected regions of Peru and identified genotype sequence type 2993, which has been associated with GBS outbreaks in China (10). These results support the hypothesis that this unprecedented GBS outbreak was related to an antecedent Campylobacter outbreak with point source. However, diarrheal illnesses shortly before or during the GBS outbreak were not reported; previous GBS outbreaks associated with Campylobacter mostly have occurred in the context of larger outbreaks of symptomatic diarrheal illness (10). Because of the wide distribution of outbreaks in many geographically separated regions, we questioned how all areas were exposed to C. jejuni within a short time frame.

Limitations of our investigation included non-systematic testing of samples and incomplete data on variables, such as hospitalization and clinical features. Epidemiologic investigations are ongoing to determine the potential antigenic source of the presumed infection, testing for Campylobacter-specific IgM and antiganglioside antibodies, additional isolate sequencing, and active surveillance for new cases.

Acknowledgments

We thank Mary Reyes, Gabriela Soto, Andree Valle, and Johans Arica for data management and quality control of the data. We also thank laboratory professionals from Regional and National Laboratories of Reference of Instituto Nacional de Salud for conducting the laboratory tests for respiratory viruses and gastrointestinal pathogens.

About the Author

Dr. Munayco is a physician, researcher, and epidemiologist at the Uniformed Services University of the Health Sciences; director of the unit of epidemiological research and evaluation of sanitary interventions at Centro Nacional de Epidemiologia, Prevención y Control de Enfermedades, Ministry of Health; and professor in the School of Medicine at Universidad Peruana de Ciencias Aplicadas. His primary research interests include public health, mathematical modeling of communicable and noncommunicable diseases, health economics, social determinants and inequality, and monitoring and evaluation of health interventions and public policies.

References

1. Sejvar JJ, Baughman AL, Wise M, Morgan OW. Population incidence of Guillain-Barré syndrome: a systematic review and meta-analysis. Neuroepidemiology. 2011;36:123–33. https://doi.org/10.1159/000324710
2. Ansar V, Valadi N. Guillain-Barré syndrome. Prim Care. 2015;42:189–93. https://doi.org/10.1016/j.pop.2015.01.001
3. Govoni V, Granieri E. Epidemiology of the Guillain-Barré syndrome. Curr Opin Neurol. 2001;14:605–13. https://doi.org/10.1010/0019052-200100000-00009
4. Nachamkin I, Arzate Barbosa P, Ung H, Lobato C, Gonzalez Rivera A, Rodriguez P, et al. Patterns of Guillain-Barré syndrome in children: results from a Mexican population. Neurology. 2007;69:1665–71. https://doi.org/10.1212/01.wnl.0000265396.87983.bd
5. Sejvar JJ, Kohl KS, Gidudu J, Amato A, Bakshi N, Baxter R, et al.; Brighton Collaboration GBS Working Group. Guillain-Barré syndrome and Fisher syndrome: case definitions and guidelines for collection, analysis, and presentation of immunization safety data. Vaccine. 2011;29:599–612. https://doi.org/10.1016/j.vaccine.2010.06.003
6. Lior H. New, extended biotyping scheme for Campylobacter jejuni, Campylobacter coli, and “Campylobacter laridis”. J Clin Microbiol. 1984;20:636–40. https://doi.org/10.1128/JCM.20.4.636-640.1984
7. Hughes RA, Cornblath DR. Guillain-Barré syndrome. Lancet. 2005;366:1653–66. https://doi.org/10.1016/S0140-6736(05)67665-9
8. Hughes RA, Rees JH. Clinical and epidemiologic features of Guillain-Barré syndrome. J Infect Dis. 1997;176(Suppl 2):S92–8. https://doi.org/10.1086/513793
9. Zhang M, Li Q, Sun H, Gu Y, You Y, et al. Genomic characterization of the Guillain-Barré syndrome-associated Campylobacter jejuni ICDCCJ07001 isolate. PLoS One. 2010;5:e15060. https://doi.org/10.1371/journal.pone.0015060
10. Zhang M, Li Q, He L, Meng F, Gu Y, Zheng M, et al. Association study between an outbreak of Guillain-Barré syndrome in Jilin, China, and preceding Campylobacter jejuni infection. Foodborne Pathog Dis. 2010;7:913–9. https://doi.org/10.1089/fpd.2009.0493

Address for correspondence: Cesar V. Munayco, Calle Daniel Olartechea 199, Jesus Maria, Lima, Peru; email: cmunayco@dge.gob.pe; James Sejvar, Centers for Disease Control and Prevention, 1600 Clifton Rd NE, Mailstop H24-12, Atlanta, GA 30329-4027, USA; email: zea3@cdc.gov
## Appendix

### Appendix Table 1. Laboratory tests and results of samples associated with Guillain-Barré syndrome, Peru, 2019*

| Sample, laboratory test              | Laboratory results |
|--------------------------------------|---------------------|
|                                      | No. tested | Positive | Negative |
| **Serum**                            |            |          |          |
| ELISA dengue IgM                     | 240        | 2        | 238      |
| qRT-PCR dengue                       | 36         | 1        | 35       |
| ELISA hepatitis E virus IgG          | 0          | 0        | 0        |
| ELISA hepatitis E virus IgM          | 0          | 0        | 0        |
| qRT-PCR Zika                         | 135        | 0        | 135      |
| ELISA Zika IgM                       | 572        | 0        | 572      |
| RT-PCR enterovirus                   | 0          | 0        | 0        |
| **Urine: qRT-PCR Zika**              | 53         | 2        | 51       |
| **Cerebrospinal fluid**              |            |          |          |
| qRT-PCR Zika                         | 46         | 0        | 46       |
| ELISA IgM Zika                       | 65         | 0        | 65       |
| qRT-PCR dengue                       | 1          | 0        | 1        |
| RT-PCR enterovirus                   | 221        | 0        | 221      |
| Enterovirus isolation                | 212        | 0        | 212      |
| FilmArray meningitis and encephalitis| 217        | 1        | 216      |
| **Nasal and pharyngeal swab samples**|            |          |          |
| IFD influenza A                       | 165        | 0        | 165      |
| qRT-PCR influenza A                  | 202        | 1        | 201      |
| IFD influenza B                       | 165        | 1        | 164      |
| qRT-PCR influenza B                  | 202        | 1        | 201      |
| qRT-PCR rhinovirus                   | 179        | 11       | 168      |
| qRT-PCR respiratory syncytial virus  | 179        | 5        | 174      |
| IFD respiratory syncytial virus      | 162        | 0        | 162      |
| qRT-PCR adenovirus                   | 177        | 2        | 175      |
| IFD adenovirus                       | 162        | 0        | 162      |
| IFD parainfluenza 1                  | 162        | 0        | 162      |
| IFD parainfluenza 2                  | 162        | 0        | 162      |
| IFD parainfluenza 3                  | 162        | 0        | 162      |
| IFD metapneumovirus                  | 164        | 0        | 164      |
| **Fecal swab**                       |            |          |          |
| Campylobacter (FilmArray gastroenteritis) | 361        | 19       | 342      |
| qRT-PCR enterovirus                  | 209        | 0        | 209      |
| Enterovirus isolation                | 162        | 0        | 162      |
| Other enteric bacteria (i.e., diarrheagenic Escherichia coli, Shigella, Salmonella) | 362        | 44       | 318      |
| **Total**                            | 5,136      | 90       | 5,046    |

*IFD, isofraxidin; qRT-PCR, quantitative real-time reverse transcription.

### Appendix Table 2. Number of other enteric bacteria isolated from fecal samples in an analysis of Guillain-Barré syndrome, Peru, 2019*

| Other enteric pathogen                  | No. |
|-----------------------------------------|-----|
| Salmonella spp.                         | 1   |
| Enteroinvasive Escherichia coli         | 11  |
| Enteropathogenic E. coli                | 1   |
| Enterotoxigenic E. coli                 | 32  |
| Shigella spp.                           | 2   |
| Nondiarrheagenic E. coli                | 157 |
| **Total**                               | 204 |
Appendix Table 3. Number of samples received by Peruvian National Institute of Health in an investigation of Guillain-Barré syndrome, Peru, 2019

| Samples                     | No. samples |
|-----------------------------|-------------|
| Feces                       | 275         |
| Nasal and pharyngeal swabs  | 394         |
| Fecal swab                  | 322         |
| Cerebrospinal fluid         | 230         |
| Urine                       | 191         |
| Serum                       | 622         |
| Other                       | 2           |
| Total                       | 2,036       |

Appendix Figure 1. Flow diagram for enrollment of cases of GBS, Peru, 2019. *Brighton levels 1 and 2 cases (n = 220) were classified as confirmed. Brighton level 3 cases (n = 463) were classified as suspected. GBS, Guillain-Barré syndrome.
Appendix Figure 2. Spatial distribution of Guillain-Barré syndrome clusters detected by kernel density, Peru, 2019.