the therapeutic approach taken to arthritis and the patient's quality of life due to poor clinical control. These drugs do not have a shared structure: the first is a recombinant protein, whereas the second is a variable fraction of a humanised monoclonal antibody. Neither do they share a therapeutic target, with one acting on T lymphocytes[1] and the other on TNF-α,[2] fundamentally produced by macrophages.

In conclusion, headache secondary to treatment with biological drugs is a well-described entity that is usually mild and associated with infusion of the drug. Our patient presented tension-type headache and headache attributed to a substance, specifically 2 biological drugs (point 8 in the third edition of the International Classification of Headache Disorders[10]); pain was refractory to pharmacological treatment and presented chronic transformation, with a significant impact on the patient's quality of life. It is important to be aware of the possibility of this adverse reaction, and it should be considered in the diagnosis of new or exacerbated headache in patients receiving disease-modifying treatment for inflammatory/autoimmune conditions. New studies with these drugs, whose complex protein structures affect functions related to the immune system, should address the reasons why they trigger headache in certain patients.

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Guillain-Barré syndrome associated with Zika virus infection in the Americas: a bibliometric study☆

Síndrome de Guillain-Barré asociado a zika, experiencia americana. Estudio bibliométrico

Dear Editor:

We conducted an extensive bibliometric study into cohorts of patients with Guillain-Barré syndrome (GBS) associated with Zika virus infection. We searched numerous databases including Scopus, Medline/PubMed, Web of Science, Science Direct, Scielo, and Imbiomed.

We selected studies conducted in the Americas and grouped them by country and cohort size; evaluated the methodology used to identify infectious agents (selecting those that screened for Zika virus as a primary objective and other agents [viruses and bacteria] as a secondary objective); and analysed the percentage of patients testing positive for Zika virus, global or average incidence, and the nerve conduction findings reported. We excluded case reports, series of fewer than 5 cases, and cohort studies not reporting serology findings for Zika virus.

We identified 22 studies analysing cohorts of patients with GBS associated with Zika virus infection, published between 2014 and 2017; cohort size varied between studies. Brazil and Colombia had the most studies published (4 and 6, respectively), followed by Puerto Rico and Mexico (3 each), and Venezuela, Jamaica, Grenada, and Martinique (one study each). We found 2 multicentre studies, with parti-

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Table 1 Main cohort studies conducted in the Americas.

Year/country	No. patients	Serology panel used	No. patients positive for Zika	Percentage patients with Zika	EMG findings	Authors
2014—2016, Brazil	57	Zika	57	100	NR	Ferreira et al.[1]
2015, Brazil	41	Zika, dengue	0	0	AMAN	Styczynski et al.[2]
2015, Brazil	38	Zika, dengue, chikungunya	18	47	AIDP	Dourado et al.[3]
2017, Brazil	35	Zika, HIV, HSV, hepatitis, CMV, syphilis, chickenpox, EBV	27	77	AIDP	Da Silva et al.[4]
2015—2016, Barranquilla, Colombia	47	Zika, dengue, HIV, CMV, *Campylobacter* (serum), syphilis, hepatitis, *Leptospira*	21	45	AIDP	Salinas et al.[5]
2015—2016, Cúcuta, Colombia	19	Zika	1	5	AMAN	Arias et al.[6]
2016, Colombia	68	Zika, dengue 1-4	17	25	AIDP	Parra et al.[7]
2016, Sucre, Colombia	23	Zika	16	70	NR	Villamil-Gómez et al.[8]
2017, Colombia	21	Zika, dengue, chikungunya	20	95	AIDP	Villa et al.[9]
2017, Cúcuta, Colombia	20	Zika, dengue, chikungunya	20	100	AIDP	Uncini et al.[10]
2016, Puerto Rico	56	Zika	34	61	AIDP	Dirlikov et al.[11]
2016, Puerto Rico	43	Zika, dengue	5	12	NR	González et al.[12]
2016, Puerto Rico	36	Zika	19	53	AIDP	Luciano et al.[13]
2016—2017, Mexico	34	Zika, dengue, chikungunya, TORCH, *Campylobacter* (rectal swab RT-PCR), HSV/enterovirus (CSF)	2	6	AIDP	Del Carpio et al.[14]
2016, Mexico	8	Zika, dengue, chikungunya	0	0	AIDP	Del Carpio et al.[15]
2017, Mexico	7	Zika, dengue, chikungunya, HIV, TORCH, hepatitis B/C, *Brucella*, *Salmonella*, *Campylobacter* (rectal swab RT-PCR), HSV/enterovirus (CSF)	0	0	AIDP	Del Carpio et al.[16]
2016, Martinique	30	Zika	23	77	AIDP	Rozé et al.[17]
2015—2016, Venezuela	30	Zika	22	73	AMSAN	Navas et al.[18]
2016, Jamaica	21	Zika, dengue, chikungunya	2	9	AIDP	Ali et al.[19]
2015—2016, Multicentre Latin America	49	Zika, dengue, HIV, CMV, hepatitis, EBV, chikungunya, herpes, *Campylobacter* (serum), *Mycoplasma*	10	20	AIDP	Ugarte et al.[20]
2015, Multicentre Latin America	24	Zika, dengue, chikungunya, rubella, measles, parvovirus	3	12	NR	Cardoso et al.[21]
2016, Grenada	9	Zika, dengue, chikungunya, West Nile virus, yellow fever, Japanese encephalitis	4	44	NR	Brenciaglia et al.[22]
Average incidence				42	AIDP	

AMAN: acute motor axonal neuropathy; AMSAN: acute motor-sensory axonal neuropathy; AIDP: acute inflammatory demyelinating polyneuropathy; CMV: cytomegalovirus; CSF: cerebrospinal fluid; EBV: Epstein-Bar virus; EMG: electromyography; HIV: human immunodeficiency virus; HSV: herpes simplex virus; NR: not reported; RT-PCR: reverse transcription polymerase chain reaction; TORCH: panel of toxoplasmosis, other, rubella, cytomegalovirus, herpes simplex virus.

cipants from different Central and South American countries (Table 1).

Two studies, conducted in Brazil and Colombia, reported Zika virus positivity in every patient with GBS; another found no case of Zika virus infection among the 41 patients studied. Incidence varied in the remaining studies.

Incidence rates were lower in Central America and the Caribbean, but the majority of studies reported rates above 50%; in North America and specifically Mexico, the incidence of positive results dropped considerably, with no association found between GBS and Zika virus infection.

The average rate of Zika virus infection in the cohorts of patients with GBS was 42%.

A meta-analysis including 3 large South American studies estimated the prevalence of GBS associated with Zika virus at 1.23%.[23]

In terms of the neurophysiological patterns reported, 12 studies reported acute inflammatory demyelinating polyneuropathy (AIDP), 2 (from Brazil and Colombia) reported acute motor axonal neuropathy (AMAN), and one (Venezuela) reported acute motor-sensory axonal neuropathy (AMSAN).

The serology tests performed vary between studies: 7 only tested for Zika virus, 5 studied the 3 main arboviruses (Zika, dengue, and chikungunya), and 3 studied Zika and dengue viruses only; others additionally searched for other viruses and bacteria, with *Campylobacter* and the TORCH panel (toxoplasma, other, rubella, cytomegalovirus, and herpes simplex) being the most frequent.

The association between Zika virus infection and GBS is variable, even between studies conducted within the same geographical region; we are therefore unable to reliably establish a causal relationship. As the Zika outbreak spread towards Central America and the Caribbean, incidence of Zika virus infection among patients with GBS decreased, approaching zero in North America.

The predominant neurophysiological pattern was AIDP. AIDP is the most frequent pattern in infectious processes and the predominant type observed in Europe and North America, whereas AMAN is usually more frequent in Mexico and Central and South America; this was not the case in these cohorts. AMSAN was predominant in a study conducted in Venezuela; this pattern has not previously been reported in the region.[24]

In conclusion, there is a need for additional clinico-epidemiological studies following a uniform protocol that may be applied and reproduced in any population; this would include testing for known pathogens of significant incidence (e.g., *Campylobacter*); major neurotropic arboviruses such as dengue, Zika, and chikungunya viruses; the TORCH panel; enteroviruses; and West Nile virus, among others.

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Guillain-Barré syndrome associated with Zika virus infection: analysis of a cohort from the region of northern Veracruz in 2016-2017☆

Síndrome de Guillain-Barré asociado a zika; análisis de la cohorte delegacional en la región Veracruz norte durante 2016-2017

Dear Editor:

We performed an observational, descriptive, retrospective study analysing cases of acute flaccid paralysis in the North Veracruz district of the Mexican Institute of Social Security in 2016 and 2017. In order to be included in the study, patients had to meet the Asbury and Cornblath criteria and Brighton criteria 1-3, and data had to be available from serological tests for arboviruses (dengue virus, Zika virus, and chikungunya virus), in accordance with the recommendations of the World Health Organization/Pan American Health Organization recommendations for the study of cases of Guillain-Barré syndrome during the arbovirus season. We also analysed the neurophysiological pattern of the disease, treatment outcomes, and mortality. Patients not meeting the inclusion criteria or not wishing to participate in the study were excluded.[1]

Patients attended in 2016 underwent testing for dengue virus (reverse-transcriptase polymerase chain reaction [RT-PCR] within 7 days of onset and IgG/IgM within 30 days), chikungunya virus (RT-PCR and IgM with a similar timeframe to testing for dengue virus), and Zika virus (serum RT-PCR within 7 days and urine RT-PCR within 14; IgG and IgM within 30 days); to identify other aetiologies, patients attended in 2017 additionally underwent an extended protocol testing for other viral and bacterial pathogens, including RT-PCR for enterovirus and herpes virus in the cerebrospinal fluid (CSF), serum IgG and IgM TORCH screen (toxoplasmosis, other agents, rubella, cytomegalovirus, and herpes simplex), and RT-PCR to detect *Campylobacter* in the stool.

The sample included 34 patients, of whom 24 were men (70.6%) and 10 were women (29.4%); 33 patients (97.1%) met the working definition for suspected Zika virus infection. CSF findings were normal in 19 patients (55.9%), with albuminocytological dissociation in 10 (29.4%) and low glucose levels in 3 (8.8%); no CSF findings were available in 2 patients (5.9%). Head CT scans were performed in 28 patients, with normal results in all cases. Neurophysiological studies identified acute inflammatory demyelinating polyneuropathy (AIDP) in 20 patients (58.8%), acute motor axonal neuropathy (AMAN) in 7 (20.6%), and acute motor-sensory axonal neuropathy (AMSAN) in one (2.9%); the study yielded normal findings in one patient (2.9%) and was not performed in 5 (14.7%). According to the Brighton criteria, the level of diagnostic certainty was level 1 in 19 patients (55.9%), level 2 in 14 (41.2%), and level 3 in one patient (2.9%). Thirty-two patients (94%) were treated with intravenous immunoglobulins (IV-Ig), one was treated with

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