

Prevalence of neurological complications associated with Zika virus in a Brazilian metropolis

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Abstract

The aim of this paper is to study the prevalence of Zika Virus (ZIKV) and the index of its neurological complications. This is a quantitative, cross-sectional epidemiological study. Data were collected through the compulsory notification of suspected ZIKV and its neurological alterations cases. 113 suspected ZIKV cases were reported, most of them in the summer, with a higher prevalence of females and in the fourth decade of life. Among the neurological changes, 15 Guillain-Barré Syndrome cases were reported, with one registered death. As neurological manifestations, most of them started 30 days after a ZIKV infection. No case has been confirmed laboratory. It is necessary to combat the vector, mainly in the summer, to reduce ZIKV infection and its neurological complications, besides instruction to the health professionals about these complications and serological tests requests for an accurate diagnosis.

Introduction

The Zika virus fever is a disease caused by a virus of the Flavivirus genus, Flaviviridae family, transmitted mainly by the *Aedes aegypti* and *Aedes albopictus* mosquitoes, being also documented the transmission by sexual relation and blood transfusion.^{1,2} Virus circulation in Brazil was laboratory confirmed in April 2015.³

Because it is a poorly described disease, its clinical characterization and natural history are based on a limited number of case reports and outbreak investigations. It is estimated that only 18% of human infections result in clinical manifestations, being, therefore, more frequent the asymptomatic infection.^{4,5} Considering that it is an emerging disease in Brazil with death, increased cases of microcephaly and neurological manifestations, these being possibly associated with the disease, the Health Surveillance Department (HSD) recommends to the State and Municipal Offices, the compulsory notification of all suspected cases, established in Ordinance No. 204 of February 17, 2016.³

The ZIKV infection clinical symptoms are nonspecific and therefore, it may be confused with other febrile diseases, especially Dengue fever and Chikungunya fever. In view of the similarity of symptoms related to febrile illness, patients do not seek health services, which contribute to the underreporting of cases.⁶

The symptoms are similar to Dengue symptoms, such as low fever (37.8°C and 38.5°C), arthralgia (on wrists and ankles, with or without edema), myalgia, headache with retro-ocular pain rashes accompanied by itching. It may also cause abdominal pain, diarrhea, constipation, photophobia, conjunctivitis and small ulcers in the oral mucosa.⁷

ZIKV protective measures recommended by the Brazilian Ministry of Health include keeping doors and windows closed or screened, wearing pants and a long-sleeved shirt, as well as the use of repellents. However, the main strategy for the reduction of the vector population requires a collective, universal and intersectoral effort.⁸

Guillain-Barré syndrome (GBS) is the largest cause of generalized flaccid paralysis in the world,^{9,10} with annual incidence of 1-4 cases per 100,000 inhabitants and peak between 20 and 40 years of age. No specific epidemiological data for Brazil, only the disease subtypes distribution.¹¹ GBS is an autoimmune disease that primarily affects the myelin of the proximal portion of the peripheral acute or subacute nerves.^{12,13}

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According to the GBS's clinical protocol and therapeutic guidelines, the risk factors identified, the disease initial stage and the fast and adequate referral for the specialized care, give to the Basic Attention an essential character for a better therapeutic result and prognosis of the cases.^{14,15}

However, it is necessary to observe the lower limbs weakness cases, reported by patients with suggestive ZIKV conditions. The GBS diagnosis is based on the lower limbs weakness clinical manifestations and also on the classic protein-cytokine dissociation in the cerebrospinal fluid. Usually, this finding is not found on the first lumbar puncture, therefore making it necessary to repeat the procedure to show the change. In some GBS cases caused by ZIKV, the appearance of clinical manifestations is early, approximately two weeks after the clinically manifested infection.⁶

For the ZIKV fever treatment are indicated rest, hydration and symptomatic treatment. The administration of non-hormonal anti-inflammatories is contraindicated. In GBS cases, they should be treated immediately in a hospital environment, and intensive therapy's support is often necessary, in which immunoglobulin use is essential.⁷

The researchers verified that the GBS estimated rate among ZIKV patients needs to be confirmed and carefully screened in order to see if the apparent increase during the ZIKV epidemic reflects a real increase and not just an increase in reporting. They

also point out that the most GBS patients in the current study reported ZIKV symptoms before the GBS onset and the majority of ZIKV cases are asymptomatic, the GBS risk may be grouped among symptomatic ZIKV infections patients.¹⁴

In 2016, 214,193 ZIKV fever probable cases in the country were evaluated, and 128,266 of these cases (59.9%) were confirmed. The incidence rate analysis of probable cases (/100 thousand inhabitants), according to geographic regions, shows that the Central-West region had the highest incidence rate: 219.2 cases/100 thousand inhabitants. In Rio de Janeiro state, 67,481 cases were reported with an incidence rate of 407.7 cases/100 thousand inhabitants. Six deaths by ZIKV were confirmed in the laboratory: 4 in Rio de Janeiro and 2 in Espírito Santo, between January and May. In relation to pregnant women, 16,923 probable cases were recorded, of which 10,820 were confirmed by clinical-epidemiological or laboratory criteria, according to Sinan-NET database.¹⁶

This study had a goal to verified the prevalence of ZIKV reports and its complications index related to neurological alterations in the Nova Iguaçu Municipal Hospital in 2016.

Materials and Methods

A quantitative cross-sectional epidemiological study, carried out in the Nova Iguaçu city, in the metropolitan region of Rio de Janeiro state, located 28 km from the state capital. It has an estimated population of 807,492 inhabitants.

The data collection was performed at the Epidemiological Surveillance of the General Hospital of Nova Iguaçu (HGNI), obtaining the notification completion sheets of the National System of Aggravation and Notifications (SINAN), from January to December, 2016. The HGNI would be the local reference for severe neurological conditions, such as those studied here.

All the ZIKV reported cases and neurological complications associated with it in the HGNI in 2016 were included in the study, where all the data present in the notifications to assemble their epidemiological profile were analyzed. Neurological abnormalities include encephalitis, meningoencephalitis, myelitis, acute flaccid paralysis and Guillain-Barré syndrome. The time between viral infection by ZIKV and the beginning of the neurological condition was also evaluated through the notification.

The data were analyzed through the ZIKV reported cases quantification and verified the cases percentage with confirmed

laboratory diagnosis. The areas where the patients lived were evaluated, having the greatest number of notifications.

The living areas were separated according to the administrative division of the city hall, which encompasses the 69 districts of the city and are then divided into the Government Regional Units in Centro; Posse; Comendador Soares; Cabuçu; Km-32; Austin; Vila de Cava; Miguel Couto; Tinguá.

We excluded from the study, neurological alteration cases where other etiological agents were confirmed, for instance, Epstein-Barr, Herpes virus, Cytomegalovirus and Campylobacter or that presented another diagnosis by the physician, such as stroke, diabetic acidosis, among others.

The study was carried out after approval by the Research Ethics Committee of the HGNI, registration number 1,615,318, CAAE 56852416.0.0000.5254. We obtained a total of 113 reports of ZIKA and 15 reports of neurological complications associated with it. The collected data were stored and analyzed using the Microsoft Office Excel 2013 program. The data were consolidated in the form of graphs and tables with absolute numbers and percentage.

Results

Zika virus

During the study, were analyzed 113 ZIKV reports, with the highest number of cases in the summer period – from January to March, with a peak in March (32 cases), showing a significant decrease in notifications in the following months, as presented in Figure 1. All the notifications analyzed had as notifiers, agents of endemics or health.

The notifications predominance was of female patients, with 62.8% of the cases whereas in the male patients, the incidence was 37.2%. The fourth decade of life was the most affected age group (21.2%), followed by the third decade of life with 18.6% of the notifications. The color evaluation was impaired since it was not filled correctly or it was marked as ignored, as well as the patients' education.

The patients living area is a relevant fact due the ZIKV be a disease with vector transmission where we must combat the transmitting agents, enabling the realization of awareness and control campaigns of the *Aedes Aegypti* vector.

When analyzing notifications for housing, it was verified that the highest inci-

dence of cases is in the region near the HGNI, in the Posse neighborhood with 41% of notifications, followed by others of patients from nearby places with 22% of report cases, verifying the result, we conclude that the hospital does not only serve the Nova Iguaçu city, but also serves the entire metropolitan region, as described in Table 1. The result found may not delimit the areas with the highest incidence of the disease in the city, since the data analyzed are limited to the HGNI, a hospital that attends urgency and emergency with medium and high complexity, which does not apply to ZIKV fever. For such delimitation, one should increase the notifications analyzed number. In the reports analyzed none of them contained confirmatory laboratory data, thus, all cases would be framed as suspect cases in the patients' clinic.

Neurological complications associated with Zika virus

Fifteen cases were reported in the analyzed period, of which 8 were women and 7

Table 1. Distribution of housing in Nova Iguaçu areas or other places of Rio de Janeiro.

Areas	N.	%
Centro	23	20.4
Posse	46	41
Comendador soares	4	3.5
Cabuçu	2	1.8
Austin	5	4.3
Miguel Couto	5	4.3
Vila de Cava	3	2.7
Outros municípios	25	22
Belford Roxo	5	
Japeri	1	
Mesquita	5	
Nilopolis	4	
Queimados	2	
Rio de Janeiro	3	
São João de Meriti	4	

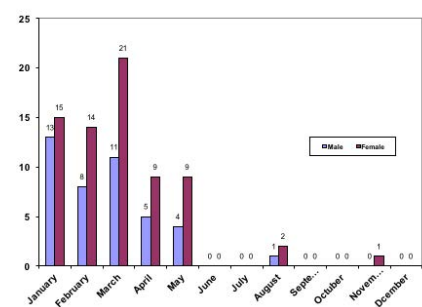


Figure 1. Distribution of Zika virus notifications in 2016 in the HGNI.

were men. As shown in Table 2, the age group with the greatest involvement was in the fourth decade of life, with 1 death also recorded in this age group.

Notifications requesting confirmatory laboratory tests for ZIKV, as recommended by the Ministry of Health, except for the request for laboratory confirmation after death were found.

Neurological signs started after 15 days (13.4%), 20 days (20%) and 30 days (33.3%) of the possible ZIKV infection, most of them with 30 days post infection. To point out, there were 5 notifications without this information (Table 2).

All reported cases were GBS, no other neurological abnormalities associated with ZIKV were reported in HGNI during 2016.

Discussion and Conclusions

The highest number of cases was reported in the summer period, showing a significant decrease in notifications in the following months, even months without notification, which corroborates the season-

ality of the ZIKV infection. This draws attention to the urgent need for educational campaigns and fight against the vector, especially in the mentioned time of the year, so conducive to infection.

It was also observed a predominance of the female sex with 62.8% of the notifications, which would probably be related to the sexual transmission of the virus, which was not observed in the other arboviruses, but could also be related only to the tendency of the women to seek more medical attention than men.¹⁷

In Brazil, a growing number of severe neurological complications among adults is related to the spread of ZIKV, according to some researches, an increase in admissions of patients with inflammatory complications such as GBS, myelitis and encephalopathy.¹⁸ Compared with a similar seasonal period prior to the first documented case of ZIKV, hospital admissions for GBS from 2015 to 2016 showed significant increases of 1.0 to 5.6 cases per month.¹⁹

In this study, a relatively high number of hospitalizations for GBS were observed, where out of 15 cases reported, 10 said to have been preceded by ZIKV infection. Most of the neurological symptoms began 30 days after ZIKV infection. None of the reports presented a result or request of the serological test for ZIKV to confirm the previous infection, except for one case where the examination was requested after the death of the patient. In cases where ZIKV had not been previously mentioned, this hypothesis could not be ruled out if it were taken into consideration that the infection could occur asymptomatic.²⁰

The notifications by GBS associated to ZIKV, except for the month of March where more cases occurred, continued to be reported with a relatively average similar in the second semester.

Nowadays there is no preventive action known that may be taken to prevent neurological injury. We expect more studies in order to find out how this ZIKV neurotropism occurs and increase awareness of its neurological complications.

Therefore, more information and instruction is required from health professionals about these complications so that they follow the recommendations of the Ministry of Health and begin to request the serology for ZIKV in all suspect cases, in order to make an accurate diagnosis. Also, it is necessary a prevention against ZIKV since we do not have much information about it and these neurological complications.

Table 2. Epidemiological profile of neurological changes reported at HGNI in 2016.

Variables	N	%
Period		
March	5	33.3
April	2	13.3
May	2	13.3
June	1	6.7
July	1	6.7
August	2	13.3
October	1	6.7
November	1	6.7
Gender		
Female	8	53.3
Male	7	46.7
Age		
10 to 20 years	1	6.7
20 to 30 years	1	6.7
30 to 40 years	6	40
40 to 50 years	3	20
60 to 70 years	3	20
70 to 80 years	1	6.7
Home		
Centro	5	33.3
Posse	3	20
Comendador Soares	1	6.7
Austin	3	20
Município de Belford Roxo	3	20
Time between onset of symptoms and ZIKV		
15 days	2	13.4
20 days	3	20
30 days	5	33.3
No information	5	33.3

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