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Application of the Surveillance Algorithm for Zika Virus in Bogota and Cali – Colombia, 2015-2017

Aplicación del algoritmo de vigilancia para el virus Zika en Bogotá y Cali (Colombia), 2015-2017

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ABSTRACT

Objective: To evaluate the application of the Surveillance algorithm for Zika of the National Institute of Health of Colombia, in newborns and pregnant women from October 2015 to June 2017 in Bogotá and Cali, Colombia. **Methods:** Descriptive study. The data were obtained from files of the National Public Health Surveillance System and the Surveillance and Follow-up Programs for children with Congenital Defects of Bogotá and Cali. Frequency of sex, affiliation to the health system and frequency of congenital defects were calculated. Compliance with the studies proposed by the algorithm and its presumptive diagnosis were analyzed. **Results:** A total of 597 records were obtained. 49.9% were male and 79% had central nervous system (CNS) abnormalities,

with microcephaly (29%) and hydrocephalus (20%). Of the pregnant women with information, Zika was positive in 16%, toxoplasmosis 4%, and CMV and syphilis each in 2%. Of the newborns, abnormalities of CNS were detected with brain ultrasound (39%), magnetic resonance imaging (38%) and computerized axial tomography (35%). **Conclusions:** The INS generated an algorithm adjusted to international surveillance parameters that allows early identification of possible complications, so its full incorporation should serve to reduce disability and mortality. The evaluation of the application of this protocol due to the multiple sources of information makes it difficult to draw definitive conclusions given the context of the Colombian health system.

Keywords
Zika virus; epidemiological monitoring; public health surveillance; congenital abnormalities; microcephaly.

RESUMEN
Objetivo: Evaluar la aplicación del algoritmo de vigilancia para Zika del Instituto Nacional de Salud de Colombia en recién nacidos y gestantes desde octubre de 2015 a junio de 2017 en Bogotá y Cali (Colombia). **Métodos:** Estudio descriptivo. Los datos se obtuvieron de fichas del Sistema Nacional de Vigilancia en Salud Pública y los Programas de Vigilancia y Seguimiento de Niños con Defectos Congénitos de Bogotá y Cali. Se calculó frecuencia de sexo, afiliación al sistema de salud y de defectos congénitos de los recién nacidos (RN); además, el cumplimiento del algoritmo y su diagnóstico presuntivo. **Resultados:** Se obtuvieron un total de 597 registros. El 49,9% de los RN fueron de sexo masculino y el 79% presentaron anomalías del sistema nervioso central (SNC), microcefalia (29%) e hidrocefalia (20%). De las gestantes con información, se reportó Zika positivo en el 16%; toxoplasmosis, en el 4%, y citomegalovirus y sífilis, cada una con un 2%. De RN con exámenes, las anomalías del SNC se detectaron con ecografía cerebral (39%), resonancia magnética (38%) y tomografía axial computarizada (35%). **Conclusiones:** El INS generó un algoritmo ajustado a los parámetros internacionales de vigilancia que permite identificar de forma temprana posibles complicaciones, por lo que su incorporación total debe servir para reducir discapacidad y mortalidad. La evaluación de la aplicación de este protocolo, debido a las múltiples fuentes de información, dificulta sacar conclusiones definitivas, dado el contexto del sistema de salud colombiano.

Palabras clave
virus de Zika; monitoreo epidemiológico; vigilancia en salud pública; anomalías congénitas; microcefalia.

Introduction

The Zika virus (ZIKV) was discovered and described on the African continent in 1947 and subsequently isolated for the first time in blood samples from a child in 1951. After this finding, new sporadic isolations of the virus were made over the years without presenting as an epidemic event (1). In 2007, the first human epidemic occurred on the islands of Yap (Federated States of Micronesia), with 48 confirmed cases and 73% of residents older than three years with serological evidence of recent ZIKV infection, with no mortality. After the outbreak in French Polynesia in 2013, ZIKV arrived on Easter Island in February 2014. A year later, an outbreak of a disease similar to dengue or chikungunya was observed in Brazil, with more than 7000 cases, around May of the same year, which were confirmed as ZIKV (1,2).

In Colombia, from the beginning of the outbreak until epidemiological week 16 of 2016, more than 13 000 pregnant women with suspected ZIKV infection were identified, with laboratory confirmation in 2008 cases. The association between ZIKV infection and congenital abnormalities of the central nervous system (CNS) was first established retrospectively in the ZIKV-affected population on Easter Island (3). During the ZIKV epidemic in Pernambuco (Brazil), ZIKV DNA sequencing was achieved in the amniotic fluid of two pregnant women, where both fetuses were previously diagnosed with microcephaly by prenatal ultrasound (4).

Subsequently, the phenotype of newborns (NB) with congenital ZIKV syndrome (n = 83) was described in Brazil. The main morphological findings were 91.6% with craniofacial disproportion, 56.6% with bilateral frontal depression, and 47% with skin folds in the occipital and nuchal regions (5). Regarding neurological symptoms, 74.7% presented hypertonia and 36.1% exhibited irritability with characteristic crying, described as "inconsolable". In the diagnostic images, it was observed that the NBs presented calcifications in 95% of the cases and more frequently in the cortico-subcortical region, with 85.5%, followed by the presence of ventricular dilatation or increase of extra-axial cerebrospinal fluid, with close to 72.3% (6).

Based on the evidence collected by the World Health Organization (WHO) and the Pan American Health Organization (PAHO), an epidemiological alert for the Americas and preliminary guidelines for surveillance of microcephaly in newborns at risk of ZIKV were issued to increase the possibility of screening and control of the disease. One of the main countries affected was Brazil, where the Ministry of Health produced the document Orientações integradas de vigilância e atenção à saúde no âmbito da emergência de saúde pública de importância nacional, while the U.S. Centers for Disease Control and Prevention produced the Interim Guidance for the Diagnosis, Evaluation, and Management of Infants with Possible Congenital Zika Virus Infection: Interim Guidance for the Diagnosis, Evaluation, and Management of Infants with Possible Congenital Zika Virus Infection, by which most affected countries have been guided to generate their surveillance and follow-up protocols (7).

The Colombian health system, in response to the ZIKV epidemic, generated the public health surveillance protocol for ZIKV disease and the notification form for "ZIKA virus disease" (INS code: 895), for appropriate follow-up, from which every fetus or newborn with a head circumference smaller than expected, according to the gestational age at birth, should be studied to determine whether the abnormality was caused by ZIKV. Additionally, in January 2016, the National Institute of Health (INS) proposed the Guidelines for the detection and comprehensive clinical management of congenital abnormalities in fetuses exposed to ZIKV during the gestation of patients in Colombia, with which it intends to make the detection and management of structural congenital abnormalities of the CNS, through the strategy of monitoring the neurodevelopment of children from birth to two years of age and determine the probable association with exposure to ZIKV. This protocol establishes that any gestational product with a structural abnormality of the CNS should be notified to initiate examinations of the mother and the newborn with RT-PCR Zika and STORCH, assessment with neuropediatrics and genetics, with a karyotype of 500 bands of resolution, transfontanelar ultrasound or computed axial tomography (CT) of the skull, radiography of the skull, long bones, spine, auditory and ophthalmologic screening. In addition, a systematic physical examination and a photographic record under the clinical practice guide for congenital abnormalities. (8)

Considering the effect of abnormalities generated by congenital ZIKV, the objective of this article is to evaluate the implementation of the algorithm developed by INS between October 2015 and June 2017, in Bogota and Cali (Colombia).

Materials and methods

A descriptive, cross-sectional, risk-free study was carried out after approval by the Research and Ethics Committee of the Faculty of Medicine of the Pontificia Universidad Javeriana, Bogotá, the Research Committee of the Faculty of Health Sciences of the Pontificia Universidad Javeriana, Cali, the Research Committee of the District Health Secretariat of Bogotá, and the Research Committee of the Health Secretariat of Cali.

This project was classified as research without risk according to Resolution 008430 of 1993 of the Colombian Ministry of Health. Since it does not involve in-person patients, there are no physical or psychological risks. Nor is the study considered to pose a risk of social, legal, or economic harm, or to require informed consent from the patients. The investigators signed a confidentiality document for the handling of the data.

The data were provided by the Bogota and Cali Health Secretariats and were supplemented with the database of the Bogotá (PVSDCB) and Cali (PVSDCC) Surveillance and Follow-up Programs for Children with Congenital Defects, with the mandatory notification form for congenital defects, congenital defects form (INS code: 215), and the form for surveillance of the Zika event, Zika virus disease (INS code: 895) of the Sivigila, from October

2015 to June 2017. The PVSDCB and PVSDCC information provides complete data from ten sentinel hospitals with case-control methodology, of which seven are located in Bogotá (Clínica Cafam de la 51, Clínica El Bosque, Clínica Veraguas, Clínica Magdalena, Hospital de Suba, Hospital San José Infantil and Hospital Universitario San Ignacio) and three in Cali (Clínica Versalles, Clínica Comfenalco and Hospital San Juan de Dios).

Inclusion criteria were all NB patients with a history of maternal exposure to Zika or with a diagnosis of microcephaly or other CNS malformations, according to the list proposed by INS Circular 004 of 2016: Q00 Anencephaly and similar congenital malformations, Q010-Q019 Encephalocele, Q02 Microcephaly, Q030-Q039 Congenital hydrocephalus, Q042 Holoprosencephaly, Q050-Q059 Spina bifida, and Q070 Arnold-Chiari syndrome.

Information from cases meeting the inclusion criteria found between October 1, 2015 and June 30, 2017, including that of the mother and father, was evaluated. The information was collected by two physicians and one technician, who received appropriate training. They verified the quality of the information, contrasting and complementing it with the patients' medical records. To this end, the staff went to the respective Primary Data Generating Unit or to the benefit plan administrators, where they searched for the information and studied each case. In addition, they made telephone calls to complete the missing information. To maintain data security and confidentiality, all data were stored in the RedCap platform provided by the Pontificia Universidad Javeriana.

The group analyzed the abnormalities of the reported cases and compliance with the tests proposed by the INS algorithm for Zika: PCR-RT for Zika and STORCH in the mother and child, assessment with neuropediatrics and genetics, 500-band resolution karyotype, transfontanelar ultrasound or CT scan of the skull, radiography of the skull, long bones, spine, hearing and ophthalmologic screening, in addition to the systematic physical examination.

According to the design of the *Congenital Defects Form* (INS code: 215), as well as the Zika virus disease surveillance form (INS code: 895), the test results for ZIKV and other infections were classified into one of the following groups: positive, negative, pending, and undetermined; the latter is defined as those for which information could not be obtained. For the reporting of the results of physical examination, diagnostic imaging, and postnatal genetic testing, the results were classified into one of the following options: normal, abnormal, in process, or undetermined, defined as those in which the information could not be obtained.

For the individual analysis, the records found for each diagnosis, their clinical correlation, and the etiological clarification of the CNS malformation were evaluated by analyzing the results with a group of clinical experts. Microsoft Excel® was used for the descriptive analysis, in which the qualitative variables were presented in tables of frequencies and percentages. This research was approved by the Ethics Committee of the Pontificia Universidad Javeriana.

Results

A total of 597 NBs were found that met the inclusion criteria. The sources of information for including the cases in the study were: 85.5% from the congenital defects form, 11% from the clinical history, and 3.5% from the Zika virus disease surveillance form. Of these newborns, 49.9% were male, 47.6% were female, and 2.3% were undetermined or unknown. With regard to the health insurance system, 65.5% of the patients were affiliated with the contributory system, 24.6% with the subsidized system, 3.7% with no affiliation, 3.7% with special affiliation, 1.3% with unknown affiliation, and 1.2% with exceptions.

The origin of the notification was mainly Bogotá (75.4%), followed by Cali (23.8%), and Boyacá and other localities (with less than 1%). Regarding the place of origin of these patients, 61.3 % corresponded to Bogotá, 20.3 % to Valle del Cauca, 5.2 % to Cundinamarca, and 13.2 %

included NBs from the departments of Cauca, Casanare, Meta, Tolima, Santander, Boyacá, Caquetá, Guainía, and Amazonas (Figure 1).

Figure 1.
Distribution of origin of patients with ZIKV in Colombia, between October 2015 and June 2017

The congenital malformations found were distributed as described in Table 1. Regarding the classification of the abnormalities by systems, the highest frequency of involvement was in the CNS, 79.3%, followed by the skeletal system, with 8.4 %, as shown in Figure 2.

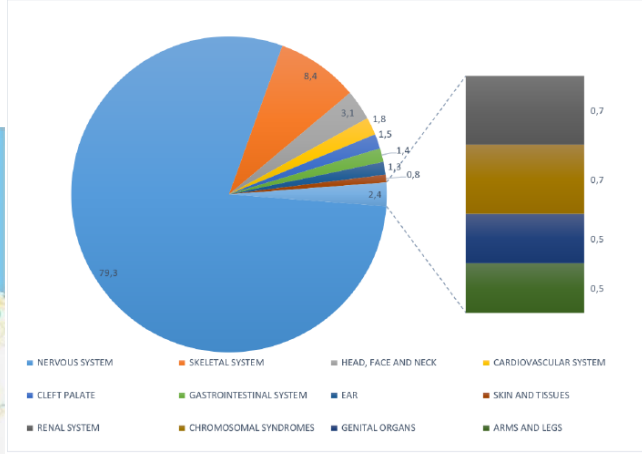

Figure 2.
Frequency of congenital abnormalities by groups related to ZIKV in newborns in Bogotá and Cali, between October 2015 and June 2017

Table 1.
Description of ZIKV congenital abnormalities in newborns in Bogotá and Cali, between October 2015 and June 2017

Abnormality	n (%)
Microcephaly	175 (29.3)
Congenital hydrocephalus	121 (20.3)
Craniosynostosis	48 (8)
Cervical spina bifida with hydrocephalus	40 (6.7)
Anencephaly	40 (6.7)
Arnold-Chiari syndrome	22 (3.7)
Holoprosencephaly	22 (3.7)
Macrocephaly	15 (2.5)
Congenital brain cysts	13 (2.2)
Atresia of the foramen of the foramina of Luschka and Magendie	10 (1.7)
Cleft hard palate and cleft soft palate	9 (1.5)
Encephalocele, unspecified	9 (1.5)
Hydrops fetalis not due to hemolytic disease	4 (0.7)
Congenital malformations of the corpus callosum	4 (0.7)
Absence, atresia or narrowing of external auditory canal	4 (0,7)
Other congenital malformations of the cerebellum	4 (0,7)
Absence, atresia and congenital stenosis of the anus, without fistula	4 (0.7)
Other specified congenital malformations of the spinal cord	3 (0.5)
Down syndrome, unspecified	3 (0.5)
Lymphagioma, of any site	2 (0.3)
Acute lymphadenitis of unspecified site	2 (0.3)
Craniorachischischisis	2 (0.3)
Congenital hydrocephalus, unspecified	2 (0.3)
Megalencephaly	2 (0.3)
Congenital malformation of the ear causing hearing impairment, not otherwise specified.	2 (0.3)
Ventriculoarterial connection discordance	2 (0.3)
Patent ductus arteriosus	2 (0.3)
Atresia of esophagus without mention of fistula	2 (0.3)
Hypospadias, unspecified	2 (0.3)
Renal agenesis, unilateral	2 (0.3)
Polydactyly	2 (0.3)
Unspecified congenital malformation of the skull and face	2 (0.3)
Congenital malformations of cardiac chambers and their connections	2 (0.3)
Congenital malformations of the peripheral vascular system	2 (0.3)
Dolicocephaly	2 (0.3)
Wernicke's encephalopathy	1 (0.2)
Diaphragmatic hernia without obstruction or gangrene	1 (0.2)
Malformations of the aqueduct of Sylvius	1 (0.2)
Congenital malformations of corpus callosum	1 (0.2)
Other specified congenital malformations of the spinal cord	1 (0.2)
Congenital malformation of the face and neck, unspecified	1 (0.2)
Common truncus arteriosus	1 (0.2)
Tetralogy of Fallot	1 (0.2)
Other penile malformations	1 (0.2)
Renal dysplasia	1 (0.2)
Congenital hydronephrosis	1 (0.2)
Phocomelia, unspecified limb(s)	1 (0.2)
Other specified osteochondrodysplasias	1 (0.2)
Other specified congenital malformations of the skin	1 (0.2)
Siamese twins	1 (0.2)
Total	**597 (100)**

Results of ZIKV-related symptoms during pregnancy were obtained in 13% of cases. It was observed that the most frequent symptom in mothers was rash (35.6%), followed by fever (28%), arthralgias (18.6%), other symptoms (20.3%), and headache (18.2%). Of the parents, 7.2% of the information on symptoms was known, with flare-up as the most frequent symptom (12.2%), followed by fever (9.5%) and arthralgias (7%).

Information was available on the performance of paraclinical tests in 14.6% of the pregnant women, diagnostic tests for STORCH and Zika in 10% of the NBs, and other specialized tests in 6.8% of the NBs. Of the results found in pregnant women, a positive result for ZIKV was reported in 16% (9); for toxoplasmosis, in 4% (4), and for CMV and syphilis, in 2% (1,2).

Regarding the 9 mothers positive for RT-PCR Zika, we found that 3 newborns had microcephaly and one had macrocephaly. The results of the newborns were positive for CMV in 4% and toxoplasma in 2%. The distribution of the specialized tests can be seen in Table 2. The karyotype was abnormal in 2% of the newborns who underwent karyotyping, while abnormal brain imaging was found in 39% of the brain ultrasound scans, 38% of the MRI scans, and 35 % of the cranial CT scans (Table 2).

Table 2.
Paraclinical results of pregnant women and newborns with congenital anomalies due to ZIKV in Bogotá and Cali, between October 2015 and June 2017

Maternal laboratory test results					
Result	**Zika**	**CMV**	**Herpes**	**Syphilis**	**Toxoplasmosis**
	n (%)	**n (%)**	**n (%)**	**n (%)**	**n (%)**
Undetermined	40 (71)	19 (37)	30 (61)	5 (6)	7 (9)
Positive	9 (16)	1 (2)	0 (0)	2 (2)	4 (4)
In process	5 (8)	0 (0,0)	0 (0)	2 (2)	1 (1)
Negative	2 (5)	32 (61)	19 (29)	77 (90)	74 (86)
Laboratory test results in newborns					
Result	**Rubella**	**CMV**	**Herpes**	**Syphilis**	**Toxoplasmosis**
	n (%)	**n (%)**	**n (%)**	**n (%)**	**n (%)**
Undetermined	26 (47)	22 (37)	28 (57)	27 (50)	23 (38)
Negative	25 (45)	32 (55)	21 (43)	27 (50)	35 (58)
In process	4 (8)	2 (4)	0 (0.0)	0 (0.0)	1 (2)
Positive	0 (0.0)	2 (4)	0 (0.0)	0 (0.0)	1 (2)
Newborn screening/testing results					
Result	**Karyotype**	**Head ultrasound**	**Head MRI**	**Head CT**	**Hearing evaluation**
	n (%)	**n (%)**	**n (%)**	**n (%)**	**n (%)**
Normal	24 (39)	13 (17)	1 (1)	3 (4)	11 (27)
Undetermined	23 (37)	37 (44)	45 (61)	45 (61)	28 (68)
In process	14 (22)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Abnormal	1 (2)	33 (39)	28 (38)	26 (35)	2 (5)

CMVcytomegalovirus; MRI: magnetic resonance imaging; CT: computed axial tomography.

Discussion

ZIKV is a virus that in recent years has been of great interest for study due to its teratogenicity in any trimester of pregnancy (9), which is associated with perinatal mortality, a wide variety of CNS defects, multiple alterations associated with ZIKV syndrome, and infant disability (10,11).

Regarding the affected newborns, this study found a predominance of CNS anomalies in male newborns, as per what was observed in a study in Colombia, in which risk factors associated with congenital defects were evaluated, where 50% of the population was male (12) and approximately 54% in the 2016 PVSACB report (13). However, in the work of Marinho et al. (14), a higher frequency of congenital defects in the female sex was reported, with 58% of the female sex in NBs with microcephaly. According to these same authors, these differences can be explained by the fact that in these studies, the same head circumference measurements were adopted for both sexes.

Regarding the health regime, in this study it was observed that the vast majority belong to the contributory regime, similar to the INS data in 2017, where they reported that 54.4% of pregnant women correspond to this regime (15).

Concerning the results of the paraclinical examinations of the pregnant woman and the newborn, it was not possible to obtain information in 90% of the cases. This could be explained by: (a) lack of resources of the health entities to perform the necessary tests that lead to confirming the etiology, as has been described in other countries in the region (10); (b) by omission in the request for tests by health personnel, which evidences ignorance or lack of adherence to protocols; (c) absence of symptoms in the pregnant women, so diagnostic tests were not taken, and (d) difficulty in collecting the results, because the pregnant women were attended in other institutions to which we did not have access. Another explanation for the RT-PCR results for Zika is that the sample was taken, but the report was not available at the time of analyzing the information for this project. It is also important to keep in mind that dengue and chikungunya are endemic in our country and present similar symptoms to Zika, which makes it difficult to follow up and adhere to protocols (16,17).

A positive ZIKV test result was found in 16% of the maternal cases in this study. A study of pregnant women in Rio de Janeiro (Brazil) discovered that 53% of pregnant women tested positive (18), whereas only 5.3% tested positive (19) in Dallas (United States). This variability can be explained by the time the test is taken, the public health policies of each country or region, the preparedness of the health sector to face an epidemic, and the knowledge of patients or health personnel about the clinical picture and the diagnosis (8).

With regard to STORCH, in this study, 4% of pregnant women were found to be positive for toxoplasmosis and 2% for cytomegalovirus and syphilis. In Colombia, it is expected that between 0.6% and 3% of pregnant women acquire toxoplasmosis during pregnancy (20), while in Europe it varies between countries: France, with 54 %, and Sweden, with 12% (21). Regarding primary maternal cytomegalovirus during pregnancy, Unicef reports a prevalence of syphilis between 0.02% and 4.5% in developed countries and between 3% and 18% in developing countries.

It was also found that for NBs, cytomegalovirus and toxoplasmosis tests were positive in 4% and 2%, respectively. Worldwide, 0.2% to 2.3% of all newborns acquire cytomegalovirus infection (22), and it is relevant to mention the association between cytomegalovirus and microcephaly, in addition to visual alterations (23). The worldwide prevalence of toxoplasmosis in newborns varies between 1 and 10 per 10,000 live births, according to the geographic area: Sweden, 1 per 10,000, Brazil, 3 per 10,000, France, 10 per 10,000, and Colombia, between 2 and 10 per 10,000 live births (24).

The data found on birth defects, including CNS defects and positive TORCH test reports, are consistent with those of other authors who have evaluated this same association. In addition,

it has been proposed that ZIKV be considered within these initial tests in pregnancy (25).

In this study, in which we recruited patients with morphological or structural alterations of the CNS, we see information coinciding with the worldwide report of the presence of CNS defects in the countries where the Zika virus outbreak occurred, among which Brazil, Argentina, and Colombia stand out (25,26,27).

When analyzing the congenital abnormalities of the newborns, microcephaly was present in more than 29% of the patients. This is consistent with studies that reported microcephaly in NBs with ZIKV-positive mothers (26). The first association studies between microcephaly and ZIKV were performed around 2015 (5). However, the spectrum of CNS abnormalities was later proven together with ZIKV syndrome (5,8).

Other CNS alterations were also found in the data studied, such as hydrocephalus (20.3%), craniosynostosis (8.0%), Arnold-Chiari syndrome (3.7%), holoproscencephaly (3.7%), brain cysts (2.2%), and atresia of the foramina of Magendie and Luschka (1.7%), consistent with that reported by other researchers, who observed CNS anomalies associated with intracranial calcifications, ventriculomegaly, polymicrogyria, and hypoplasia of the corpus callosum and cerebellum (7, 28).

Regarding neural tube defects, in this study, spina bifida and anencephaly were present in 6.7% of cases, and encephalocele in 1.5%. Other countries have reported high prevalences of neural tube defects not associated with ZIKV. However, in general, an increase in these defects was observed in the periods associated with this epidemic in different regions (29).

In the diagnostic images of the newborns, it was found that ultrasonography showed abnormalities in 39% of the cases in which it was performed, as well as in 38% of magnetic resonance imaging and 35% of head CT. These results are similar to those found by Levine et al. (7), who compared the findings of congenital defects in fetuses with mothers positive for ZIKV and TORCH through the use of ultrasonography.

Regarding the strategy for surveillance and follow-up of the ZIKV emergency in Colombia, the INS developed the public health surveillance protocol for ZIKV disease and the notification form for Zika virus disease, which were very similar to those adopted in Brazil, Spain, and the United States.

The two differences found in the Colombian protocol are the non-inclusion of the immunoglobulin M test for dengue, which could be explained by the high prevalence of this disease and, therefore, the high probability of cross-reactivity with flavivirus (30), and the inclusion of a karyotype of at least 500 bands in version 2 of the protocol for Intensified Surveillance of Microcephaly and other Congenital Defects of the Central Nervous System. In our study, only one karyotype was found with an abnormal result, corresponding to 2%, which generated a hypothesis of no association between Zika and chromosomal abnormalities.

The prevalence of ZIKV congenital syndrome could not be accurately determined in the present study; however, this data could be improved in the proposed follow-up registry. In Brazil, a rate of 8 per 10,000 live births was reported for congenital ZIKV syndrome (10), being the highest prevalence reported, and in the United States, 7 per 10,000 live births for the same period (26).

Conclusions

We can conclude that the development of a surveillance protocol for an emerging event such as Zika or other potential teratogens is critical for the management and monitoring of an epidemic.

The algorithm developed by the INS is considered complete and is in line with the international surveillance parameters for these cases. In this scheme, the initial decision to follow up is based on the suspected case by obstetric ultrasound. In addition to the case with microcephaly, clinical examinations, imaging, and paraclinical tests are recommended, which contribute to the management of patients, optimize the resources allocated to their care, and probably, by early identification of possible

complications, reduce severity, disability, and mortality.

During the evaluation of the algorithm, it was not possible to analyze the frequency of compliance due to the fragmentation of the information, possibly secondary to the different affiliations with the insurance companies, the disintegrated care of the patients, and the taking of exams in different health care institutions, in addition to a variable adherence to the protocol by the health care personnel, explained by multiple factors, which made the availability of the information difficult.

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Conflict of interest

The authors have no conflicts of interest to declare.

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In posthumous tribute to Dr. Paula Hurtado, for her friendship, human quality, dedication to service and dedication to medicine, teaching, and research.

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