

# **Seminario 78: Zika y Embarazo**

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# Zika y Embarazo

- Arbovirus, familia Flaviviridae, género Flavivirus
- Incluye
  - Dengue
  - Fiebre amarilla
  - Virus del Oeste del Nilo
  - Chicungunya
- Virus ARN monocatenario
- 2 Linajes
  - África: transmisión entre primates no humanos por mosquito
  - Asia: humano es el principal huésped
- Mutación en el linaje asiático ha hecho que se adapte al humano

# Zika y Embarazo

- Picadura diurna (amanecer – anochecer)
  - Saliva de Mosquito Aedes Aegypti
  - Zona Urbana
  - Interior y/o exterior
- Sexual
  - Detección de RNA viral en semen desde día 17 hasta día 62 desde inicio de sintomatología
- Transplacentaria y perinatal
  - RNA en líquido amniótico y muestras de sangre pareada entre madre e hijo
- No hay evidencia de transmisión por saliva, orina o gotitas respiratorias

# Zika y Embarazo

- Se ha detectado virus en:
  - ◆ Orina
  - ◆ Sangre
  - ◆ Semen
  - ◆ Líquido cefalorraquídeo

# Virus Zika: Clínica

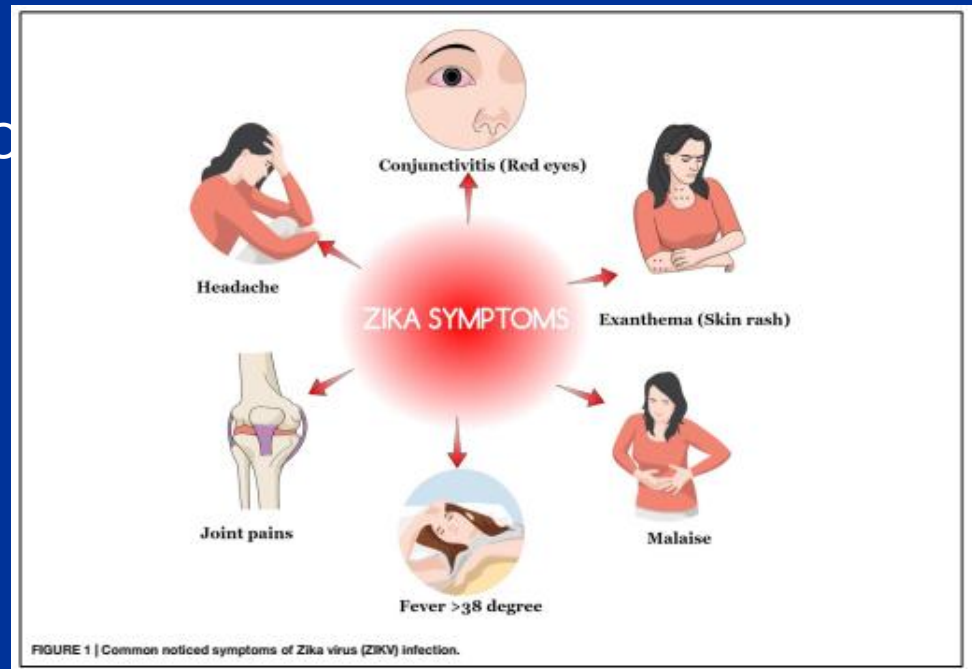
- Subclínica: 80%
- Enfermedad leve
- Período de incubación: 3 - 12 días
- Duración sintomatología: 2 a 7 días



Basarab M, Bowman C, Aarons EJ, et al.  
Zika virus. *Bmj* 2016;352:i1049.

# Sintomatología

- OMS: Sospecha de infección aguda:
  - ◆ Rash o Fiebre ( $>37,2 <38,5$  °C) mas:
    - ★ Artralgia o mialgia
    - ★ Conjuntivitis no purulenta
    - ★ Hiperemia conjuntival (específica)
    - ★ Cefalea
    - ★ Compromiso del estado general
- Otros síntomas:
  - ◆ Dolor retro-orbitario
  - ◆ Edema periférico
  - ◆ Gastrointestinales





Clinical Practice and Quality

# Zika Risk and Pregnancy in Clinical Practice

*Ongoing Experience as the Outbreak Evolves*

*Rashmi Rao, MD, Stephanie L. Gaw, MD, PhD, Christina S. Han, MD, Lawrence D. Platt, MD, and Neil S. Silverman, MD*

**Table 2. Clinical Findings and Screening Results**

	Yes (%)	95% CI	Other
Ultrasound findings (n=173)	5 (2.9)	1.1–6.2	12*
Bites (n=185)	123 (66.5)	59.4–73.0	3 <sup>†</sup>
Symptoms (n=185)	19 (10.2)	6.5–15.3	8 <sup>‡</sup>
Rash	10 (53)		
Fever	9 (47)		
Conjunctivitis	3 (16)		
Headache	5 (26)		
Myalgias	5 (26)		
IgM testing ordered (n=153)	141 (92.2)	87.1–95.6	
PCR testing ordered (n=153)	12 (7.8)	4.4–12.9	
Public laboratory (n=153)	109 (71.2)	63.7–78.0	
Commercial laboratory (n=153)	44 (28.8)	22.0–36.3	

CI, confidence interval for proportions; IgM, immunoglobulin; PCR, polymerase chain reaction.

\* Ultrasound evaluation was not indicated at the time of the visit.

<sup>†</sup> Patients in whom mosquito bites were possible but patient was unsure.

<sup>‡</sup> Patients who reported more than one symptom.

Obstet Gynecol. 2017 Jun;129(6):1098-1103

# Zika y Diagnostico

- Estudio de ácidos nucleótidos: Sangre y suero hasta 7 días de iniciado la sintomatología ( ideal <5 días). Orina desde 6 a 10 días
- Serología (Detección de IgM) : Sangre o suero mas de 7 días hasta 2- 12 semanas
- Prueba de reducción por neutralización de placas: dado reacción cruzada



# Zika y diagnostico

- Rol del PCR en liquido amniótico y sangre de cordón aun no esta determinado
- Se ha realizado estudio inmunohistoquímicos en placentas y abortos

## REVIEW ARTICLE

Lindsey R. Baden, M.D., *editor*

## Zika Virus

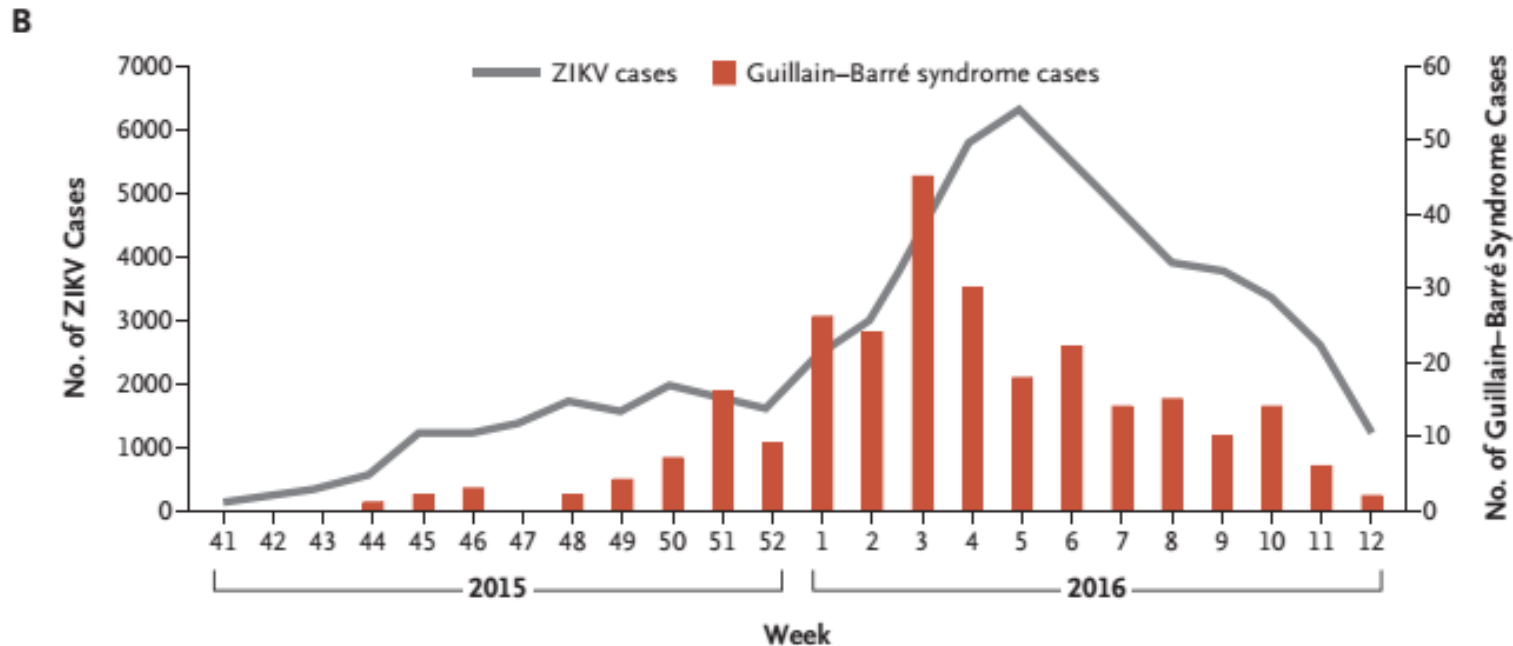
Lyle R. Petersen, M.D., M.P.H., Denise J. Jamieson, M.D., M.P.H.,  
Ann M. Powers, Ph.D., and Margaret A. Honein, Ph.D., M.P.H.

**N Engl J Med 2016;374:1552-63.**

# Zika y Síndrome de Guillian Barré

- 2013-2014: Polinesia francesa reportó un 88 % de SGB asociación con virus Zika. OR >34
- 2015 : Brasil reportó 62 % asociación con virus Zika

# Zika y Síndrome de Guillian Barré



**Figure 1. Cases of ZIKV Infection and the Guillain-Barré Syndrome in Colombia.**

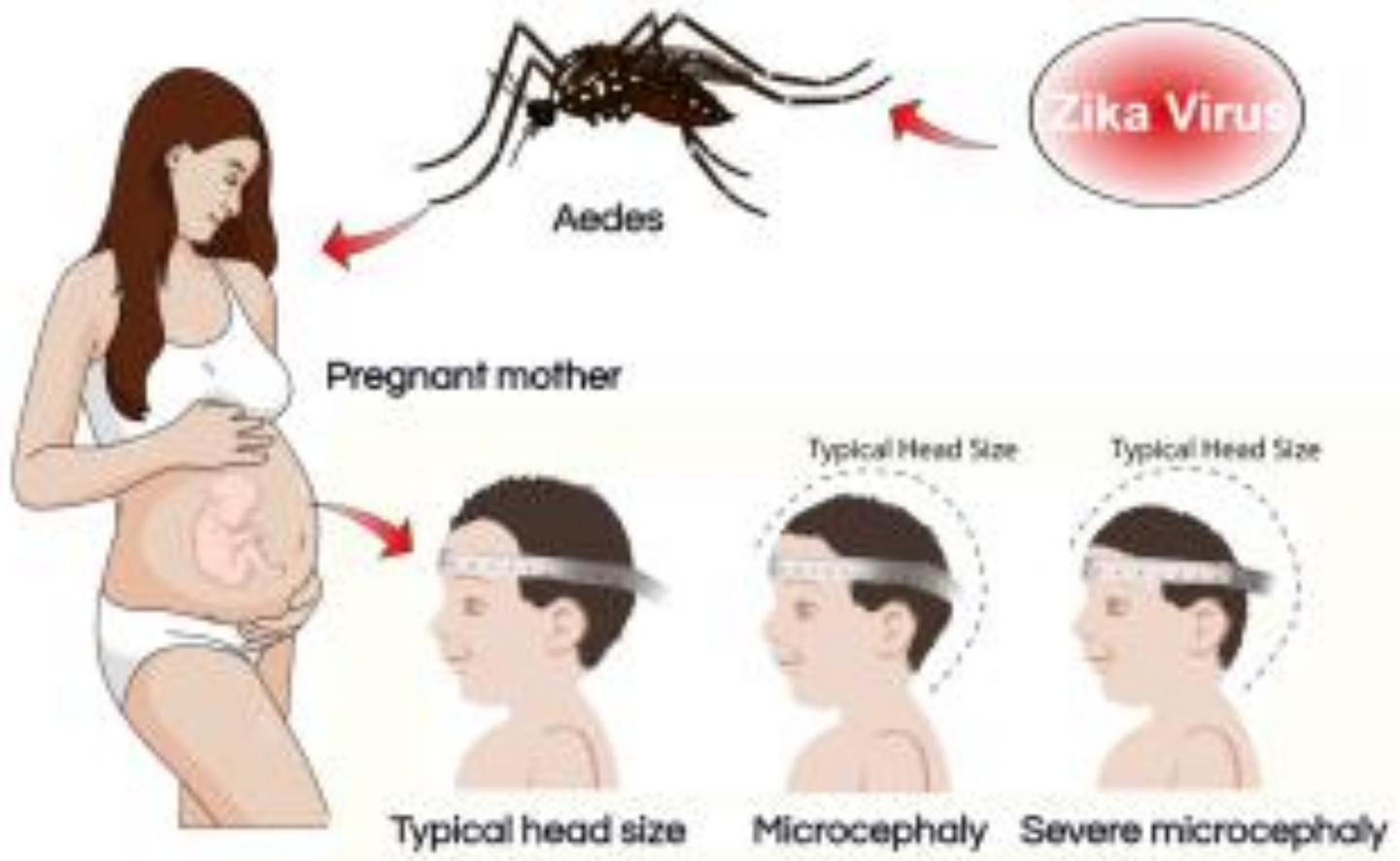
Panel A shows a map of Colombia with Neuroviruses Emerging in the Americas Study (NEAS) participating sites in the context of the Zika virus (ZIKV) infection outbreak. Numbers of confirmed cases of ZIKV infection from epidemiologic week 32 of 2015 through week 12 of 2016 are shown. Panel B shows the cases of the Guillain-Barré syndrome that were diagnosed in parallel with ZIKV cases reported to the Colombian National Institute of Health and epidemiological surveillance system in Colombia from October 2015 through March 2016.

# Zika y alteraciones neurológicas

- Se ha reportado asociación con meningoencefalitis y mielitis

Mécharles S, Herrmann C, Poullain P, et al. Acute myelitis due to Zika virus infection. Lancet 2016 March 3

Carteaux G, Maquart M, Bedet A, et al. Zika virus associated with meningoencephalitis. N Engl J Med 2016;374:1595-6



# Vital Signs: Update on Zika Virus— Associated Birth Defects and Evaluation of All U.S. Infants with Congenital Zika Virus Exposure — U.S. Zika Pregnancy Registry, 2016

TABLE 1. Pregnancy outcomes\* for 972 women with completed pregnancies<sup>†</sup> with laboratory evidence of possible recent Zika virus infection, by maternal symptom status and timing of symptom onset or exposure — U.S. Zika Pregnancy Registry, United States, December 2015–December 2016

Characteristic	Brain abnormalities and/or microcephaly (No.)	NTDs and early brain malformations, eye abnormalities, or consequences of CNS dysfunction without brain abnormalities or microcephaly (No.)	Total with ≥1 birth defect (No.)	Completed pregnancies (No.)	Proportion affected by Zika virus-associated birth defects, % (95% CI <sup>§</sup> )
<b>Any laboratory evidence of possible recent Zika virus infection<sup>¶</sup></b>					
<b>Total</b>	43	8	51	972	5 (4–7)
<b>Maternal symptom status</b>					
Symptoms of Zika virus infection reported	18	3	21	348	6 (4–9)
No symptoms of Zika virus infection reported	24	4	28	599	5 (3–7)
Unknown	1	1	2	25	—
<b>Timing of symptoms or exposure<sup>**</sup></b>					
First trimester <sup>††,§§</sup>	13	1	14	157	9 (5–14)
Multiple trimesters including first	22	6	28	396	7 (5–10)
<b>Confirmed evidence of Zika virus infection<sup>¶¶</sup></b>					
<b>Total</b>	18	6	24	250	10 (7–14)
<b>Maternal symptom status</b>					
Symptoms of Zika virus infection reported	8	3	11	141	8 (4–13)
No symptoms of Zika virus infection reported	10	2	12	102	12 (7–19)
Unknown	0	1	1	7	—
<b>Timing of symptoms or exposure<sup>**</sup></b>					
First trimester <sup>††,§§</sup>	8	1	9	60	15 (8–26)
Multiple trimesters including first	8	4	12	58	21 (12–33)

- Aproximadamente el 5 % de los recién nacidos presentara alguna malformación congénita en las embarazadas con sospecha de infección
- Aumento a 10 % en pacientes con diagnostico confirmado de infección
- Sin diferencia de presencia o ausencia de sintomatología materna
- 84 % de las anomalías congénitas corresponde a microcefalia y alteraciones SNC

- No hay evidencia de asociación con malformación fetal en madres expuesta en el segundo y tercer trimestre
- Contrariamente Brasil et al. Encontró riesgo segundo y tercer trimestre
- Se ha detectado microcefalia desde 18- 20 semanas



**Box. Birth Defects Potentially Related to Zika Virus Infection During Pregnancy and Monitored by the US Zika Pregnancy Registry for Enhanced Surveillance**

**Brain Abnormalities With and Without Microcephaly**

Confirmed or possible congenital microcephaly<sup>a</sup>

Intracranial calcifications

Cerebral atrophy

Abnormal cortical formation (eg, polymicrogyria, lissencephaly, pachygyria, schizencephaly, gray matter heterotopia)

Corpus callosum abnormalities

Cerebellar abnormalities

Porencephaly

Hydranencephaly

Ventriculomegaly/hydrocephaly (excluding "mild" ventriculomegaly without other brain abnormalities)

Fetal brain disruption sequence (collapsed skull, overlapping sutures, prominent occipital bone, scalp rugae)

Other major brain abnormalities including intraventricular hemorrhage in utero (excluding postnatal intraventricular hemorrhage)

# Malformaciones del SNC

**Neural Tube Defects and Other Early Brain Malformations**

Neural tube defects including anencephaly, acrania, encephalocele, spina bifida

Holoprosencephaly (arhinencephaly)

**Eye Abnormalities**

Microphthalmia/anophthalmia

Coloboma

Cataract

Intraocular calcifications

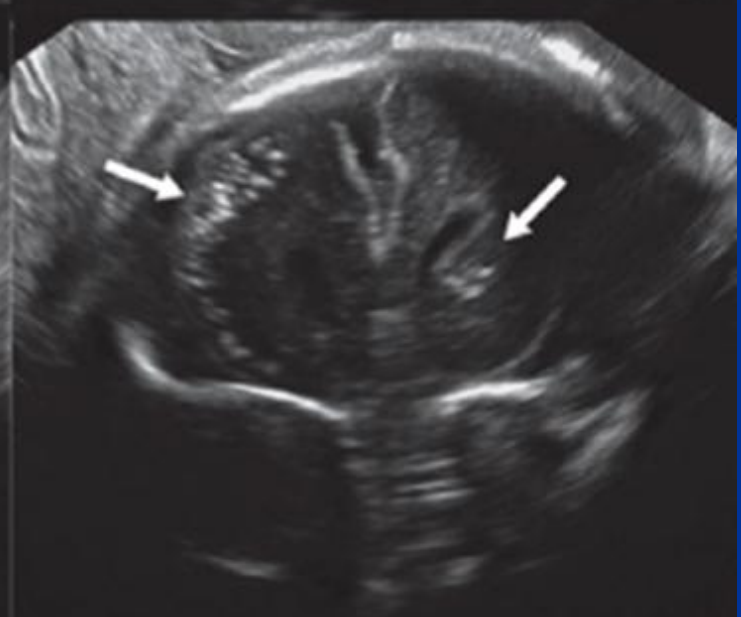
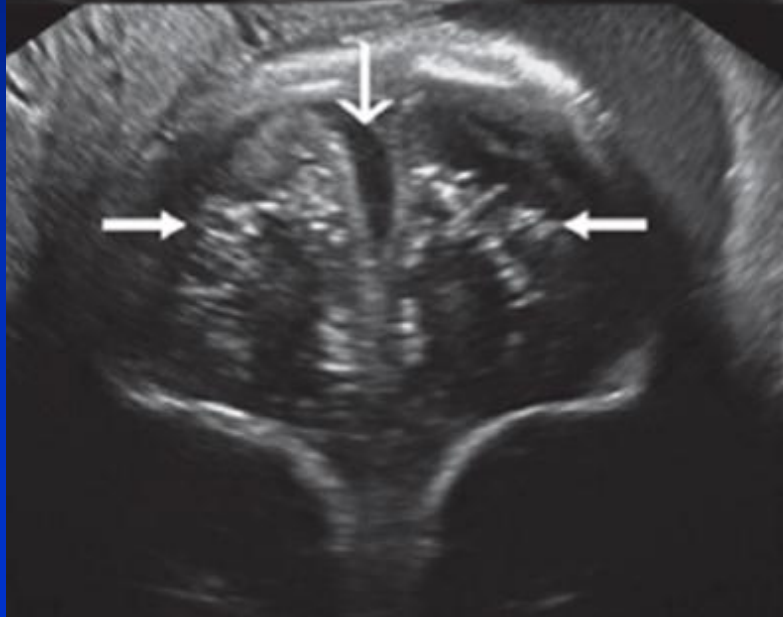
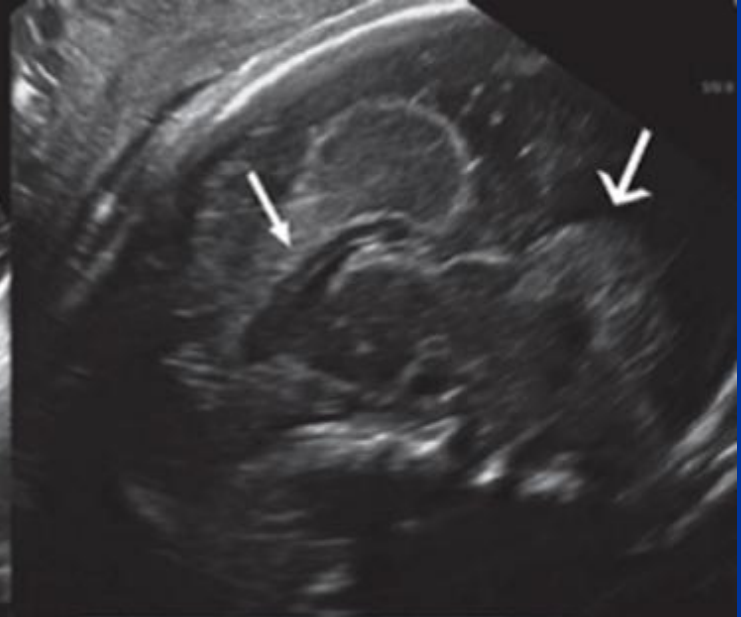
Chorioretinal anomalies involving the macula (eg, chorioretinal atrophy and scarring, macular pallor, gross pigmentary mottling and retinal hemorrhage; excluding retinopathy of prematurity)

Optic nerve atrophy, pallor, and other optic nerve abnormalities

**Consequences of Central Nervous System Dysfunction**

Congenital contractures (eg, arthrogryposis, clubfoot, congenital hip dysplasia) with associated brain abnormalities

Congenital deafness documented by postnatal audiological testing



**Table 2. Pregnancy Outcomes According to ZIKV Exposure.**

Variable	ZIKV-Positive Women (N=134)	ZIKV-Negative Women (N=73)	P Value
	<i>no. of women/total no. (%)</i>		
Lost to follow-up before birth of infant	9/134 (6.7)	12/73 (16.4)	0.003
Known pregnancy outcomes	125/134 (93.3)	61/73 (83.6)	0.03
Live births, including one set of twins	116/125 (92.8)	57/61 (93.4)	1.00
Adverse pregnancy outcomes*	58/125 (46.4)	7/61 (11.5)	<0.001
Fetal loss	9/125 (7.2)	4/61 (6.6)	1.00
During first trimester	5/125 (4.0)	3/61 (4.9)	0.72
Rate per total no. of first-trimester maternal infections	5/20 (25)	3/4 (75)	0.72
During second trimester	2/125 (1.6)	0/61	1.00
Rate per total no. of second-trimester maternal infections	2/71 (2.8)	0/35	1.00
During third trimester	2/125 (1.6)	1/61 (1.6)	1.00
Rate per total no. of third-trimester maternal infections	2/34 (5.9)	1/22 (4.5)	1.00
Adverse pregnancy outcomes including fetal loss			
First trimester	11/20 (55.0)	3/4 (75.0)	<0.001
Second trimester	37/72 (51.4)†	2/35 (5.7)	<0.001
Third trimester	10/34 (29.4)	2/22 (9.1)	<0.001
Obstetrical complications‡	42/107 (39.3)	20/57 (35.1)	0.62

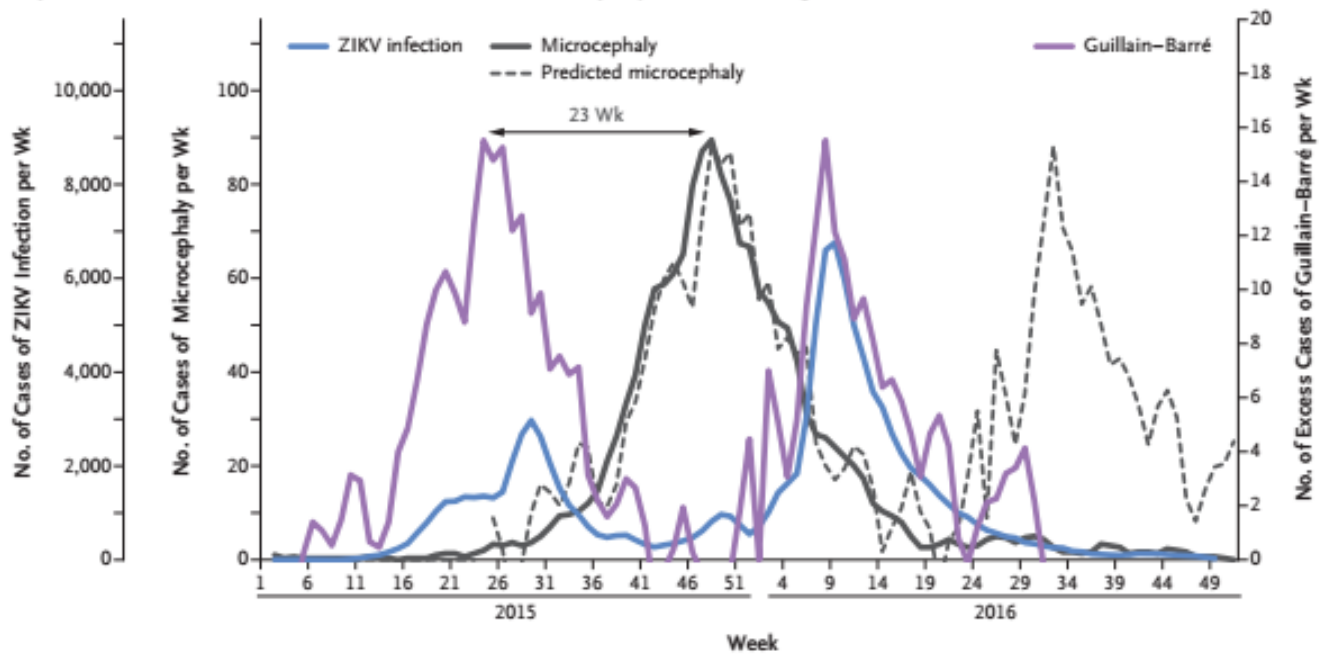
# Pronostico

Zika Virus Infection in Pregnant Women in Rio de Janeiro . NEJM 375;24

<b>Alteraciones ecográfica n (%)</b>	<b>12 (29%)</b>
<b>RCIU</b>	<b>5</b>
<b>Calcificaciones cerebrales</b>	<b>4</b>
<b>Alteraciones de AU y ACM</b>	<b>4</b>
<b>Otras alteraciones del SNC</b>	<b>2</b>
<b>OHA y anhidroamnios</b>	<b>2</b>
<b>Microcefalia</b>	<b>4</b>

Brasil P, Pereira JP, Gabaglia CR et al Zika Virus Infection in Pregnant Women in Rio de Janeiro – Preliminary Report, NEJM, 4 March 2016

**B Suspected Cases of ZIKV Infection, Guillain–Barré, and Microcephaly in Northeast Region**



**Figure 1.** Suspected Cases of Zika Virus (ZIKV) Infection, Guillain–Barré Syndrome, and Microcephaly in Brazil (2015–2016). Panel A shows the suspected cases of ZIKV infection that were reported weekly in clinics and hospitals in the five regions of Brazil during 2015 and 2016. Panel B shows the suspected cases of ZIKV infection, Guillain–Barré syndrome (GBS), and microcephaly in 2015 and 2016, along with the predicted cases of microcephaly in 2015 and 2016. The suspected cases of GBS are reported as excess cases — that is, the numbers of cases that surpass the average number reported each week in the years before the ZIKV epidemic (in 2010 to 2014). In 2015, the incidence of microcephaly followed the identification of ZIKV infection and GBS by an interval of 23 weeks on average. However, there was no predicted resurgence of microcephaly after the apparent seasonal increases in the incidence of ZIKV infection and GBS in 2016. Case series in Panels A and B are plotted as 3-week moving averages. Data were collected by the Ministry of Health in Brazil.

# Disminución de los casos previstos

- Menos casos de los previstos
  - ◆ Mutación Virus?
  - ◆ Cofactor asociado ?
  - ◆ Reacción cruzada ?

**PREGNANT WOMAN**

Assess for possible Zika virus exposure  
Evaluate for signs and symptoms of Zika virus disease

**A**

**B**

- Symptomatic : <2 weeks after symptom onset, or
- Asymptomatic and NOT living in an area with active Zika virus transmission: <2 weeks after possible exposure

- Symptomatic: 2–12 weeks after symptom onset, or
- Asymptomatic and NOT living in an area with active Zika virus transmission: 2–12 weeks after possible exposure, or
- Asymptomatic and living in an area with active Zika virus transmission: 1st and 2nd trimester

Zika virus NAT on serum and urine

Zika virus IgM and dengue virus IgM on serum

Positive Zika virus NAT on serum or urine:  
*Recent Zika virus infection*

Negative Zika virus NAT on serum and urine

Dengue virus IgM positive or equivocal and Zika virus IgM negative:  
*Presumptive dengue virus infection*

Zika virus IgM positive or equivocal and any result on dengue virus IgM:  
*Presumptive recent Zika virus or flavivirus infection*

Zika virus IgM and dengue virus IgM negative:  
*No recent Zika virus infection*

- Symptomatic: Zika virus IgM and dengue virus IgM
- Asymptomatic and NOT living in an area with active Zika virus transmission: Zika virus IgM 2–12 weeks after exposure.

Zika virus IgM and dengue virus IgM negative:  
*No recent Zika virus infection*

Zika virus IgM or dengue virus IgM positive or equivocal  
*Presumptive recent Zika virus or dengue virus or flavivirus infection*

Reflex Zika virus NAT on serum and urine

Plaque reduction neutralization test (PRNT)

Negative Zika virus NAT on serum

Positive Zika virus NAT on serum or urine:  
*Recent Zika virus infection*

Zika virus PRNT  $\geq 10$  and dengue virus PRNT <10:  
*Recent Zika virus infection*

Zika virus PRNT  $\geq 10$  and dengue virus PRNT  $\geq 10$ :  
*Recent flavivirus infection, specific virus cannot be identified*

Zika virus PRNT <10:  
*No recent evidence of Zika virus infection*