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SHORT COMMUNICATION

Chikungunya, Zika and Dengue seroprevalence rates among pregnant women in a hospital of southeastern Brazil

Soroprevalência de chikungunya, zika e dengue em gestantes de um hospital do sudeste do Brasil

Seroprevalencia de chikungunya, zika y dengue en mujeres embarazadas en un hospital del sureste de Brasil

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Corresponding Author:
Bernardo Bastos Wittlin
bernardo.bw@gmail.com

Avenida Marechal Campos, 1000, Universitário, CEP 00000-000, Santa Cruz do Sul, RS, Brasil.

Bernardo Bastos Wittlin[1];
Dalziza Victalina de Almeida[1];
Bianca Cristina Leires Marques[1];
Carolina Cipriano Monteiro[2];
Luiz Felipe de Souza Moreira[2];
José Henrique Rezende Linhares[1];
Rosalina Jorge Koifman[3];
Sheila Maria Barbosa de Lima[1];
José Henrique Pilotto[1];

[1] *Instituto Oswaldo Cruz, FIOCRUZ, Rio de Janeiro, RJ, Brasil.*
[2] *Hospital Geral de Nova Iguaçu Nova Iguaçu, Rio de Janeiro, Brasil.*
[3] *Escola Nacional de Saúde Pública Sérgio Arouca (ENSP), Manguinhos, RJ, Brasil*

ABSTRACT

Background and objectives: For decades, dengue outbreaks have been affecting vast territories of the Americas. In 2010's decade, Chikungunya and Zika virus (CHIKV and ZIKV) emerged as new arboviruses in the region. While several seroprevalence rates have been reported for dengue virus (DENV) infection in Brazil, serological surveys for the latest are scarce. We aimed to evaluate the seroprevalence of CHIKV, ZIKV, and DENV infections in pregnant women at admission to a public maternity hospital of Nova Iguaçu, state of Rio de Janeiro. **Methods**: A simple questionnaire was applied, containing limited demographic, obstetric, and clinical data, alongside with blood collection. Different commercial test kits, based on enzyme-linked immunosorbent assay (ELISA), were used. **Results**: Among 349 pregnant women enrolled from July to December 2017, there was a 28.4% seroreactivity for CHIKV, 47.2% for ZIKV, and 88.8% for DENV. **Conclusion**: These findings reflect the high dengue endemicity scenario and suggest a significant reach of the recent outbreaks of ZIKV and CHIKV infections in the region.

Keywords*: Chikungunya Fever. Zika Virus Infection: Dengue. Seroepidemiologic Studies. Pregnant women.*

RESUMO

Justificativas e objetivos: Há décadas, surtos de dengue afetam vastos territórios das Américas. Na década de 2010, os vírus Chikungunya e Zika (CHIKV e ZIKV) surgiram como arbovírus emergentes na região. Embora diversas taxas de soroprevalência tenham sido relatadas para a infecção pelo vírus da dengue (DENV) no Brasil, pesquisas sorológicas para chikungunya e zika são escassas. Objetivou-se avaliar a soroprevalência das infecções por CHIKV, ZIKV e DENV em gestantes admitidas em uma maternidade pública de Nova Iguaçu, estado do Rio de Janeiro. **Métodos**: Foi aplicado um questionário simples, contendo dados demográficos, obstétricos e clínicos limitados, sendo realizada

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coleta de sangue na mesma visita. Diferentes kits de teste comerciais, baseados em ensaio imunoenzimático (ELISA), foram utilizados. **Resultados**: De 349 gestantes recrutadas de julho a dezembro de 2017, houve sororreatividade de 28,4% para CHIKV, 47,2% para ZIKV e 88,8% para DENV. **Conclusão**: Esses achados refletem o cenário de alta endemicidade da dengue e sugerem um alcance significativo dos surtos recentes causados por ZIKV e CHIKV na região.

***Descritores**: Febre de Chikungunya. Infecção pelo vírus Zika. Dengue. Estudos Soroepidemiológicos. Gestantes.*

RESUMEN

Justificación y objetivos: Durante décadas, los brotes de dengue han afectado a vastos territorios de las Américas. En la década de 2010, los virus Chikungunya y Zika (CHIKV y ZIKV) surgieron como arbovirus emergentes en la región. Aunque se han reportadas varias tasas de seroprevalencia para la infección por el virus del dengue (DENV) en Brasil, la investigación serológica para el chikungunya y el Zika es escasa. Este estudio tuvo como objetivo evaluar la seroprevalencia de infecciones por CHIKV, ZIKV y DENV en mujeres embarazadas ingresadas en una maternidad pública en Nova Iguaçu, estado de Rio de Janeiro. **Métodos**: Se aplicó un sencillo cuestionario, que contenía datos demográficos, obstétricos y clínicos limitados, y se extrajo sangre en la misma visita. Se utilizaron diferentes kits de prueba comerciales basados en el ensayo inmunoabsorbente ligado a enzimas (ELISA). **Resultados**: De 349 mujeres embarazadas reclutadas de julio a diciembre de 2017, hubo serorreactividad de 28,4% para CHIKV, 47,2% para ZIKV y 88,8% para DENV. **Conclusión**: Estos hallazgos reflejan el escenario de alta endemicidad para el dengue y sugieren una variedad significativa de brotes recientes causados por ZIKV y CHIKV en la región.

***Palabras clave**: Fiebre Chikungunya. Infección por el virus del Zika. Dengue. Estudios seroepidemiológicos. Mujeres Embarazadas.*

During the early 2010s, Chikungunya and Zika virus (CHIKV and ZIKV) were introduced and spread throughout the Americas, leading to large outbreaks.[1] Like Dengue virus (DENV) besides several other arboviruses, ZIKV and CHIKV are transmitted to humans by *Aedes* spp. mosquitoes, superimposing public health challenges toward historically dengue endemic regions. These arboviral infections are known to cause health complications to newborns of infected mothers, even in asymptomatic maternal infection involving preterm delivery, fetal anomalies, low birth weight, and miscarriage.[2, 3]

While several seroprevalence rates have been reported for dengue in Brazil, serological surveys for chikungunya and zika infections are still scarce. This study aimed to evaluate the serological prevalence of CHIKV, ZIKV, and DENV among pregnant women in a public maternity hospital in the state of Rio de Janeiro, Brazil.

We conducted a cross-sectional study at the Hospital Municipal Mariana Bulhões, located in the municipality of Nova Iguaçu. The city is part of the Baixada Fluminense region, northwest of the state capital, and had approximately 800,000 inhabitants in 2017, with a low-to-middle socioeconomic index. While being the only public maternity hospital in Nova Iguaçu, it provides maternal-infant care to the neighboring municipalities and performs around 5,000 deliveries per year.

As eligibility criteria, we defined any pregnant women, above 18 years old, who were admitted to the emergency/pre-delivery room. We excluded women presenting severe/unstable clinical conditions at admission. Sample size calculation was based on the average of deliveries for the recruitment period, which occurred from July to December 2017, through a convenience sampling. A simple questionnaire was applied, containing limited demographic, obstetric, and clinical data. Self-reported previous history of dengue, zika, and chikungunya infections, as well as yellow fever vaccination, were probed. Acute arboviral suspect cases were defined on a clinical basis. Blood samples were collected at the same visit. Samples were assayed in duplicate with ELISA commercial kits for dengue, zika, and chikungunya, performed according to manufacturer instructions. "Borderline" results were considered as negative for this analysis. These included: Anti-DENV IgM (Serion Elisa Classic - Virion\Serion, Germany); Anti-DENV IgG (Euroimmun, Germany); DENV NS1 antigen (Panbio Dengue Early ELISA, South Korea); Anti-ZIKV IgM capture (Novagnost, Germany); Anti-ZIKV IgG (Euroimmun, Germany); Anti-CHIKV IgM and Anti-CHIKV IgG (Euroimmun, Germany).

This study was approved by the Instituto Oswaldo Cruz Ethics Committee (protocol number: 66996217.7.2002.5254). All participants signed an informed consent form.

A total of 349 pregnant women were enrolled, with no exclusions or refusals to participate. The average age was 26.9 years (Table 1). The average gestational age was 38.8 weeks. Participants came from different parts of the city, especially from the central and populous zones. Approximately 36% came from neighboring municipalities. Most pregnant women were admitted in labor (81%). No participants presented clinical manifestations of acute arboviral infections. When asked about the history of dengue, zika, and chikungunya, there were affirmative answers in, respectively, 6%, 12%, and 9% of the cases. Out of 168 participants who were asked about previous vaccination against yellow fever, only one answered affirmatively.

From the 349 specimens submitted to the different commercial ELISA tests, there were 163 IgG positive and 6 IgM positive specimens for ZIKV, corresponding to 47.2% (95% CI: 42.0 to 52.5) of seroreactivity. The positivity for DENV occurred in 310, corresponding to 88.8% (95% CI: 85.5 to 92.1). All specimens were negative for DENV NS1

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Table 1. Demographic and obstetric data of pregnant women in a public maternity hospital in Nova Iguaçu (RJ), from July to December 2017 (n = 349).

Variable	Category	n (%)
Age (years)	18-24	141 (40.4)
	25-29	100 (28.7)
	29-47	108 (30.9)
Municipality of origin	Nova Iguaçu	222 (64)
	Belford Roxo	36 (10)
	Mesquita	12 (3)
	Queimados	38 (11)
	Japeri	17 (5)
	Other municipalities	19 (6)
	No data	5 (1)
Gestation trimester	First trimester	2 (<1)
	Second trimester	2 (<1)
	Third trimester	332 (95)
	Indeterminate / no data	13 (4)
Prenatal care	Yes	310 (89)
	No	12 (3)
	No data	27 (8)
Reason for hospital admission	Labor	282 (81)
	Suspected arboviral infection	0 (0)
	Other reasons	58 (17)
	No data	9 (2)

antigen. As for CHIKV, 99 of the specimens had positive IgG, and none had positive IgM; thus, it corresponded to 28.4% (95% CI: 23.6 to 33.1) (Table 2).

Despite being a convenience sampling, serological surveys involving pregnant women recruited from health services are a good tool, since may offer a glimpse of the general population's actual seroprevalence. Moreover, most of the Baixada Fluminense population is assisted by the public health system, like the participants in our study.

In comparison with two other chikungunya serological surveys carried out during 2017 in Brazil, our finding is superior to that of Netto et al.[4] in Salvador (7.4%), and that of Cunha et al.[5] in Riachão do Jacuípe (20%), both cities in the state of Bahia. Concerning zika, Netto et al.[4] found even higher seroprevalence in Salvador (63.3%), highlighting a subgroup of 273 pregnant women with 69.3%, recruited between 2015-2016. In another study involving blood donors in São Paulo state, Slavov et al.[6] demonstrated ZIKV seroreactivity obtained in 2015, 2016, and 2017 of 5.3%, 12.8% and 13.2%, respectively. Another study has found 61.3% of ZIKV IgG positive among mothers who gave birth between 2015 and 2016, during the peak of zika fever and microcephaly outbreak in Recife, Pernambuco state.[7] As for dengue, we have found a seroprevalence rate that approximates those most remarkable from population-based studies conducted in Brazil (4.0-91.1%).

Among the limitations of this study, there are the possible cross-reactions involving antibodies against DENV and ZIKV. This phenomenon typically occurs among flaviviruses and has long been known, leading to false positives in serological tests.[8] Neutralizing antibody tests, not used in this study, have been used in serological surveys, increasing specificity, and reducing this problem. The commercial test for ZIKV used herein is based on the non-structural protein NS1, generally considered more specific than certain targets of the envelop glycoprotein E.[9] Some studies reported satisfactory accuracy for this test,[10, 11] while one did not.[12]

Finally, these results reflect a scenario of dengue high endemicity in Baixada Fluminense, pointing out to the deficiency of vector control policies in recent decades. This context favored the emergence of *Ae. aegypti*-related new arboviruses, like chikungunya and zika, with high impact on public health. While showing significant seroprevalence, it also suggests the possibility of new and imminent epidemic waves, taking into account the observed proportion of susceptibility in our sample.

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Table 2. Results of ELISA tests for DENV, ZIKV and CHIKV among 349 pregnant women in a public maternity hospital in Nova Iguaçu (RJ), from July to December 2017.

Virus	Serology	Commercial test	Positive n (%)	Borderline n (%)	Negative n (%)	Seroprevalence n (%)	CI (95%)
DENV	IgM	Virion\Serion	32 (9.2)	39 (11.1)	278 (79,7)	310/349 (88.8)	85.5% - 92.1%
	IgG	Euroimmun	308 (88.3)	4 (1.1)	37 (10.6)		
	NS1	Panbio	0 (0.0)	-	349 (100.0)		
ZIKV	IgM	Novagnost	6 (1.7)	8 (2.3)	335 (96.0)	165/349 (47.2)	42.0% - 52.5%
	IgG	Euroimmun	163 (46.7)	39 (11.2)	147 (42.1)		
CHIKV	IgM	Euroimmun	0 (0.0)	3 (0.9)	346 (99.1)	99/349 (28.4)	23.6% - 33.1%
	IgG	Euroimmun	99 (28.4)	4 (1.1)	246 (70.5)		

DENV - dengue virus; ZIKV- zika virus; CHIKV - chikungunya virus

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AUTHORS' CONTRIBUTIONS

Bernardo Bastos Wittlin and José Henrique Pilotto contributed to the design;

Bernardo Bastos Wittlin, Dalziza Victalina de Almeida and Carolina Cipriano Monteiro contributed to the formal analysis;

José Henrique Pilotto and Sheila Maria Barbosa de Lima contributed to the acquisition of the financing;

Bernardo Bastos Wittlin and Luiz Felipe Moreira contributed to the investigation; Bernardo Bastos Wittlin, Bianca Cristina Leires Marques, José Henrique Rezende Linhares, Sheila Maria Barbosa de Lima and Rosalina Jorge Koifman contributed to the methodology;

José Henrique Pilotto and Dalziza Victalina de Almeida contributed supervision and review.

All authors have approved the final version to be published and are responsible for all aspects of the work, including ensuring its accuracy and integrity.