

Final Abstract Number: 21.001

Session: Hot Topics in Infection and Prevention Control

Date: Friday, March 2, 2018

Time: 17:00–18:00

Room: Libertador C

Type: Invited Presentation

The World Health Organization (WHO) clean care is safer care promotion campaign, 2005-2018



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The World Health Organization (WHO) *Clean Care is Safer Care* global programme is based around a change model. It fosters partnerships and coordinates activities as set out in its programme plan. By May 2016, more than 140 of the 194 United Nations' member states had pledged their support to implement actions to reduce healthcare-associated infections, corresponding to 95% coverage of the world population.

The finalized WHO Guideline on Hand Hygiene in Healthcare was launched in 2009 alongside a field-tested and validated multimodal improvement strategy. The strategy comprises five critical components: 1) system change; 2) healthcare workers' training and education; 3) evaluation and performance feedback; 4) reminders in the workplace; and 5) promotion of an institutional safety climate.

WHO has over this time coordinated more than 50 national campaigns and importantly launched the global annual healthcare worker call to action; the SAVE LIVES: Clean Your Hands campaign to maintain a profile on hand hygiene action at the point of care.

Reasons for the success of *Clean Care is Safer Care* will be reviewed, including those possibly associated with a positive influence on infection rates and patient safety.

<https://doi.org/10.1016/j.ijid.2018.04.3531>

Final Abstract Number: 22.001

Session: Oral Presentations: Arboviruses

Date: Friday, March 2, 2018

Time: 17:00–18:00

Room: Retiro A

Type: Oral Presentation

Maternal immunity and antibodies to dengue can promote Zika virus-induced microcephaly in fetuses



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Background: Zika virus (ZIKV), a recently emerged flaviviral pathogen, has been linked to microcephaly in neonates. Yet, it is not understood why some fetuses develop severe microcephaly due to maternal ZIKV infection while others do not. The risk for ZIKV-induced microcephaly is greatest during the first trimester of pregnancy in humans, yet this alone cannot account for the varied presentation of microcephaly observed. Given the antigenic similarity between ZIKV and closely related dengue virus (DENV), combined with the substantial immunity to DENV in ZIKV target populations in recent outbreaks, we hypothesized that maternal

antibodies against DENV were a risk factor for ZIKV-induced microcephaly.

Methods & Materials: Using immune-competent mice, we developed a mouse model of maternal to fetal transmission of ZIKV infection. Mother mice were infected on embryonic day 7 (E7), an equivalent fetal developmental stage to the first trimester of human pregnancy. Microcephaly was assessed in the fetuses by measuring head circumference and cortical thickness on E18, near full-term. ZIKV replication was measured in the mothers and fetuses by real-time quantitative PCR, negative-strand PCR, and immunohistochemistry for multiple ZIKV proteins. To test the influence of DENV immunity on fetal infection, mothers that were DENV immune or that were given the flavivirus cross-reactive monoclonal antibody 4G2 were infected with ZIKV and their fetuses were examined. Mice deficient in the neonatal Fc receptor (FcRN), which is known to carry maternal antibodies into the fetus, were used to determine its role in vertical transmission of ZIKV infection.

Results: We observed disproportionate microcephaly and reduced cortical thickness in the fetuses of ZIKV-infected mothers, which was greatly enhanced by DENV immunity or 4G2-injection of mother mice. ZIKV infection was also enhanced by DENV-specific antibodies both in fetuses and in the mothers' spleens. Use of FcRN-deficient mice showed that there was significantly increased trans-placental infection in an FcRN-dependent manner, leading to a greater incidence of microcephaly in the fetuses of DENV-immune mothers.

Conclusion: We show that DENV-specific antibodies in expectant mothers results in a severe microcephaly like-syndrome during ZIKV infection. Furthermore, fetal infection was promoted by FcRN. Our results raise caution since ZIKV epidemic regions are also endemic to DENV.

<https://doi.org/10.1016/j.ijid.2018.04.3532>

Final Abstract Number: 22.002

Session: Oral Presentations: Arboviruses

Date: Friday, March 2, 2018

Time: 17:00–18:00

Room: Retiro A

Type: Oral Presentation

Neurodevelopmental delays arising from in utero exposure to Zika virus in Salvador, Brazil



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Background: Since 2015, Brazil has experienced an unprecedented Zika virus outbreak. A devastating consequence of this viral infection is congenital Zika infection (CZI), which is transmitted from pregnant women to newborns. Most descriptions and publications regarding CZI focus on the clinical presentation of newborns and infants with microcephaly. Scarce information is available concerning children without microcephaly born from infected mothers.

During 2016, in the city of Salvador (Bahia, Brazil), a cross-sectional study enrolled 103 pregnant women who reported an exanthematous disease during pregnancy. Of these, 69 (67%)

presented anti-Zika antibodies at the time of delivery. A total of 7 (6.8%) newborns were diagnosed with microcephaly, while 96 (93.2%) were classified as newborns without microcephaly.

Methods & Materials: In June 2017, we began a prospective follow-up of these infants without microcephaly exposed to Zika Virus *in utero* by evaluating neurodevelopment delays, performing neurological examinations and applying the Bayley Scales of Infant Development III (BSID-III), Mental Development Index (MDI) and Bayley-III cognitive and language scales. Auditory evaluations were performed by Otoacoustic emissions (OAE) and Brainstem Auditory Evoked Potential (BAEP).

Results: To date we have evaluated 18 infants, mean age 1.7 years. Of these, 55.6% are male and 61% were delivered by C-section. Anti-Zika IgG serology was positive in 75% and three (16.6%) presented positivity for Zika by PCR on urine samples within 24 h of birth. Based on head circumference (HC) at time of birth, all were classified as normal by the Intergrowth scale and currently fall within normal HC percentiles. Cognitive delay was identified in five (33%) infants, language delay in four (26.6%) and motor delay in two (13.3%).

Conclusion: Our preliminary results indicate that *in utero* exposure to Zika virus could be associated with neurodevelopmental delay, even in children born without microcephaly at birth. Currently, only microcephalic infants are referred to specialized care, while normocephalic children are maintained in primary health care. We believe that all newborns exposed to Zika *in utero* should be referred to specialized centers for the early detection of neurodevelopmental delays and timely intervention.

<https://doi.org/10.1016/j.ijid.2018.04.3533>

Final Abstract Number: 22.004

Session: Oral Presentations: Arboviruses

Date: Friday, March 2, 2018

Time: 17:00-18:00

Room: Retiro A

Type: Oral Presentation

Neurological complications associated with arboviruses during Zika outbreak in Salvador, Bahia-Brazil



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Background: An unprecedented and concurrent outbreak of Dengue (DENV), Chikungunya (CHIKV) and Zika (ZIKV) virus happened in Brazil in 2015. Approximately 18.372 cases of an acute exanthematous illness were notified in Salvador, Bahia and several cases of Guillain-Barré Syndrome (GBS) raised.

Methods & Materials: We started a hospital surveillance for GBS and other neurological syndromes in two general hospitals in Salvador, northeastern Brazil.

Results: Twenty-seven cases were included, of which 18 (66%) were female. The mean age was 40 years and 26 (93%) of them had acute symptoms suggestive of arbovirus infection before the onset of neurological symptoms. The main symptoms were skin rash, pruritus, myalgia, and fever. The median time between onset of acute

symptoms and neurological symptoms was 10.5 days. Seventeen cases (63%) were classified as GBS, 3 (11%) as acute encephalitis, 2 (7%) as opsoclonus-myoclonus ataxia syndrome (OMS), 2 (7%) as myelitis, 1(4%) as Carpal tunnel syndrome and 1 (4%) as acute disseminated encephalomyelitis (ADEM). GBS cases presented in a variety of clinical spectrum, with 8 (47%) as acute ataxic neuropathy, 5 (29%) as classic GBS, 2 (11%) as bifacial weakness with paraesthesias, 1 (5%) as paraparetic GBS and 1 (5%) as classic Miller-Fischer syndrome. Twelve (44%) patients were admitted to semi-intensive or intensive care units and none died. The arbovirus diagnosis was established in 21(77.8%) of the cases. Serological evaluation by ELISA singly detected IgM-specific DENV antibodies in 3 cases (2 SGB and 1 Myelitis), IgM-specific CHIKV antibodies in 4 cases (3 SGB and 1 myelitis) and IgM-specific ZIKV antibodies in 3 cases (SGB). Six cases had both anti-ZIKV and anti-DENV (2 SGB, 2 encephalitis, 1 ADEM, 1 OMS) with a presumptive ZIKV diagnosis. One case of OMS had a coinfection by CHIKV and DENV-4 established by RT-PCR.

Conclusion: Herein, we describe 28 cases of GBS and other neurological syndromes associated with arboviruses. Besides GBS, we also identified cases of encephalitis, ADEM and OMS, a rare syndrome characterized by chaotic eyes movement and ataxia. Thereafter, clinicians and health care providers should be aware of the potential severe neurological complications associated with arbovirus infection in epidemic areas.

<https://doi.org/10.1016/j.ijid.2018.04.3534>

Final Abstract Number: 22.005

Session: Oral Presentations: Arboviruses

Date: Friday, March 2, 2018

Time: 17:00-18:00

Room: Retiro A

Type: Oral Presentation

Projecting the end of the Zika epidemic in Latin America: A modelling analysis



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Background: Zika virus disease emerged in Latin America in early 2015, which had serious implications for population health. In 2016, the World Health Organization declared a cluster of neurological disorders and neonatal malformations associated with Zika cases a Public Health Emergency of International Concern. 2017 incidence has declined, and future disease incidence in Latin America remains uncertain due to gaps in our understanding of the natural history of infection, considerable variation in surveillance and a lack of a comprehensive collation of available data from affected countries.

Methods & Materials: This analysis combines publically available data on Zika virus incidence across most Latin American countries and a spatio-temporal dynamic transmission model for Zika virus infection to determine key transmission parameters and likely future incidence in 87 cities. Seasonality was determined by spatio-temporal estimates of *Aedes aegypti* vector capacity. Country and state-level data are used to infer key model parameters using Monte-Carlo methods, different movement models were tested against the data and the best-fitting parameter combinations were used to estimate incidence within each city.

Results: We predict that the highest incidence in 2018 will be observed in Colombia and some Brazilian States (Parana, Sao Paulo, Rio de Janeiro and Minas Gerias), but the estimated number of