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An Integrated Intervention Model for the Prevention of Zika and Other *Aedes*-Borne Diseases in Women and their Families in Mexico

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Additional information is available at the end of the chapter

<http://dx.doi.org/10.5772/intechopen.71504>

Abstract

We describe and discuss the rationale, design and current implementation of a model for an integrated intervention for the primary and secondary prevention of Zika and other *Aedes*-borne diseases and sexually transmitted infections that impact reproductive health, pregnancy and perinatal life stages in women and their families in Merida, Mexico. The intervention includes enhanced surveillance of pregnant women, implementation of communication strategies to promote good practices to prevent disease transmission, determination of the frequency of structural anomalies detected prenatally in the foetus, umbilical cord and placenta of pregnancies diagnosed with ZIK infection, detection of ZIKV and other arboviruses/viruses in products of abortion, in-utero and early newborn, provision of *Aedes aegypti*-proof houses" (protecting homes with door/window screens with insecticide to prevent the access of mosquitoes), mosquito repellents, larvicides and education/promotion of best practices for the prevention of infection with dengue (DENV), chikungunya (CHIKV) and Zika (ZIKV) and an anthropological studies on sociocultural factors of pregnant women associated with ZIKV. This intervention is being developed in a population of 10,000 people of the city of Merida and with the participation of a multidisciplinary group of public health professionals in collaboration with the Ministry of Health and the Government of Yucatan.

Keywords: Zika, dengue, chikungunya, prevention, *Aedes*-borne diseases, *Aedes aegypti*, intervention, house screening, sexual transmission, pregnant women

1. Introduction

Dengue (DEN), chikungunya (CHIK) and now Zika (ZIKV) are *Aedes*-borne diseases (ABD) in different transmission stages in southern Mexico, that is, endemic (DEN), epidemic (CHIK) and emergent (ZIKV), that account for increasing number of cases, chronic disability conditions and deaths along with the threat of increasing numbers of congenital disorders. While ABD face the operational problems associated to the control the mosquito vector *Aedes aegypti*, ZIKV infection has also a non-vectorial transmission route: vertical (transplacental and birth), sexual and/or by blood transfusion which may compromise the health of the mother, fetus and the newborn [1].

The first outbreak of ZIKV outside of Africa and Asia was in Micronesia and affected 72% of the population in 2007 [2] and was confirmed by Centers for Disease Control and Prevention (CDC) [2, 3]. Transmission of (ZIKV) spread to Malaysia, the Philippines and French Polynesia. In 2013–2014, French Polynesia reported a ZIKV outbreak reaching 60% of the population [2–5]. In 2015, Brazil had an outbreak of ZIKV with 134,057 confirmed cases, were fatal and 80% were asymptomatic [6]. Colombia reported more than 65,000 positive cases of ZIKV during the first half of 2016 [7]. The outbreak of ZIKV in Mexico started at the end of 2015 in Chiapas where 8842 confirmed cases were reported by June of 2017. The Yucatan state, also in south Mexico, has reported 1295 cases and most of confirmed Zika infections in pregnant women (921 confirmed cases) in Mexico [6, 8, 9].

Recent ZIKV epidemiological alerts associate ZIKV/pregnancy with fetal/neonatal morbidity and mortality because there was a marked increase in newborns that developed microcephaly during the ZIKV outbreak in Brazil. By the end of 2015, detection by RNA sequencing of ZIKV from amniotic fluid of foetuses with disorders in the central nervous system was the key for the World Health Organization (WHO) to declare the ZIKV a public health emergency [10–12]. Actually, congenital Zika syndrome (CZS) involves craniofacial malformations (microcephaly, craniofacial anomalies and facial dysmorphism), foetal brain disruption sequence and neural tube defects [13–16]. DEN and CHIK as well, are associated with spontaneous abortion, prematurity and congenital diseases, and the newborn may present thrombocytopenia, hepatomegaly and develop neurological disorders.

The virus has been documented in body fluids as blood, tears, breast milk, vaginal discharge, semen and tissues from abortions and stillbirths [17, 18]. Confirmation of infectious diseases through laboratory diagnostic tests are often necessary; the arrival of ZIKV infection made that the tools developed for other flaviviruses such as DEN, based on immune response (IgM, IgG), would generate false positives to ZIKV. There are several working groups that are developing more specific and sensitive IgM and IgG tests, so it is essential to be definite of the final

diagnosis, due to the possible consequences that could involve a false positive or false negative diagnosis. The polymerase chain reaction (PCR) has become the main mechanism for the diagnosis of ZIKV nuclei acid; however, compared to the viral particles of DEN and CHIK, the viral particles of ZIKV are low and therefore the period to give a positive diagnosis in serum is very short and challenging. Other possibilities are detection in urine saliva, breast milk and semen, in pregnant women and their spouses, where a longer viremia is reported [17–20].

This situation challenges vector control and the surveillance system, the prevention of transmission and the organization of health care systems that should effectively deal with the concurrence of three diseases with different clinical outcomes and a common vehicle of transmission. Major challenges include the establishment of a comprehensive communication strategy to sensitize and provide information regarding the risk of ZIKV infection in pregnant women, and the early detection and confirmation of arboviral diseases in the target group (pregnant women) in order to launch the preventive and control interventions. Additional challenges include the improvement or prenatal, pregnancy and newborn care in primary health care centers and hospitals as well as strengthening the surveillance of ABD in these areas.

We need to implement integrated strategies that can improve detection of infection and special medical care for infected women, the follow-up of newborn at risk and the best preventive and vector control measures. Herein, we describe and discuss the design and current implementation of an integrated model for primary and secondary preventive interventions for ZIKV, along with other ABD and sexually transmitted infections, that impact reproductive health, pregnancy and perinatal life stages in women and their upspring in Merida, Mexico.

We describe the rationale, components, implementation and evaluation of this intervention, which includes:

- Enhanced surveillance of pregnant women, including the early detection of infectious diseases such as syphilis, HIV and DEN/CHIK/ZIKV.
- Implementation of communication strategies, that is, prevention and control measures against the bite of the mosquito vectors, family-planning strategies.
- Determination of the frequency of structural anomalies detected prenatally in the fetus, umbilical cord and the placenta of pregnancies affected by infection with ZIKV.
- Detection of ZIKV, and other arboviruses/viruses in products of abortion, in-utero and early newborn.
- Implementation of the strategy “Casas a prueba de *Aedes aegypti*/*Aedes aegypti*-proof houses” in Yucatan (protecting homes and families with door/window screening to prevent the access of mosquitoes), provision of mosquito repellents and larvicides, and education/promotion of best practices for the prevention of infection with DEN, CHIK and ZIKV.
- Conducting an anthropological research of sociocultural factors associated with Zika virus.

2. Enhanced surveillance of pregnant women, including the early detection of infectious diseases such as syphilis, HIV and DEN/CHIK/ZIKV

In Merida, a strong collaborative work with local authorities is already in place with interventions targeting high-risk areas and vulnerable populations. These efforts were initially organized for DEN control due to its endemic transmission in the area. Due to the introduction of CHIK in early 2014, and the most recent introduction of ZIKV, the program has extended to address these three ABD with major emphasis in ZIKV infection due to its high impact in the newborn. “Familias sin Dengue project” (**Figure 1**) (financed by SANOFI-Pasteur) has established a platform for the surveillance and early detection of dengue infection that will be used to improve detection of ZIKV infection in target women.

2.1. Surveillance of ZIKV and urban *Aedes*-borne diseases (ABD) with in the cohort study “Familias sin dengue”

For Merida, the team has access to datasets containing the residential address of ~25,000 DEN and ~5000 CHIK cases reported during 2011–2016 including the study area. The Cohort study: “Familias sin Dengue” also provides a group of women in reproductive age who will be followed through house visits in order to detect suspicion of ZIKV infection.

ZIKV infection in the general population presents with a mild disease that remit in 3–7 days. ABD are endemic in Yucatan, and congenital infections result from the transmission of



Figure 1. Identification logo of the project families without dengue.

infection from the mother to the foetus during pregnancy. Therefore, in populations with an epidemiological association of ZIKV, pregnant women should be intentionally evaluated for ZIKV during the development of clinical manifestations similar to those described [11]. It is essential to establish a correct diagnosis in the pregnant woman due to the poor information generated on the transmission, pathophysiology and diagnosis of the impact that this infection has on the product of gestation [10, 21].

The virus in addition to being identified in saliva, blood, semen, urine, in breast milk, has also been found, but it is not known, if breastfeeding can affect the baby. But if vertical transmission has been demonstrated through amniocentesis, with confirmation the presence of ZIKV by PCR and reported lesions vary according to the time of infection and time of pregnancy. However, information about ZIKV infection proximate to the conception period is scarce. Women who are positive should have a follow-up for the search for morphological abnormalities in their products. Zika infection in the mother with transmission to the fetus, causing a group of structural abnormalities of at least the central nervous system (CNS), which produces a sequence of cerebral disruption and causes a functional disability secondary to damage, is denominated congenital Zika syndrome (CZS) [13, 22–24].

Enhanced surveillance searches for prenatal and/or neonatal morphological abnormalities in all products of pregnancies affected by ZIKV. This performed by perinatologists specialized in fetal medicine and geneticists from the dysmorphological approach. A family history is made of all the patients with the purpose of obtaining a history of genetic diseases or the use of teratogens that may imply in the diagnosis of maternal-fetal health.

According to the guidelines established by the CDC, there is no optimal time to perform an ultrasonographic screening to detect microcephaly. On a daily basis, ultrasound surveillance to detect structural abnormalities in a pregnancy is performed among the 18–20 weeks of gestation [25]. Ultrasonographic follow-up should be performed from the beginning of the ZIK symptomatology in the mother with a monthly monitoring depending on the prenatal manifestations found. The variables investigated are intrauterine growth, cephalic perimeter, central nervous system abnormalities and other structural abnormalities as well as the presence of intracerebral and/or placental calcifications and the amount of amniotic fluid.

Upon ultrasonographic findings of malformations in the product, the patient will be informed, who will decide whether or not to follow the pregnancy. In case of a request for the interruption of the pregnancy the case will be evaluated by a Bioethics Committee to define the resolution.

Pregnancies with or without ZIKV infection that culminate in abortion or early foetal death, with prior informed consent, will be performed a genetic clinical evaluation, with collection of body images, and evisceration or autopsy will be performed, as the case may be, to obtain brain tissue, hepatic, cardiac and renal, to perform histopathological study and RT-PCR for ZIKV nuclei acid in frozen and fixed tissue. The mother will be informed of the findings and genetic counseling on care and risk will be given to reduce birth defects in subsequent pregnancies. To date, there is no contraindication to vaginal delivery and breastfeeding.

2.2. Studies for the core group

The core group of the study are the pregnant women of two interventions; the cohort study (**Figure 2**): “families without dengue” (**Figure 1**) and “*Aedes aegypti*-proof houses” (**Figure 3**) in which previous informed and signed consent, with clarity the commitments that the group of professionals, as well as the participant and their family have.

When a pregnant woman, her partner and family enter the project, the following diagnostic tests and complementary studies are carried out (**Figure 4**):

- A. Molecular detection of ZIKV is performed with the use of the Trioplex Real time RT-PCR Assay from the Centers for Disease Control and Prevention (CDC), for detection and differentiation of RNA from DEN, CHIK and ZIKV in serum and urine, to all members of the family.
- B. Serum and urine studies with Trioplex RT-PCR monthly to the pregnant woman and her partner throughout pregnancy.
- C. HIV and VDRL (syphilis) tests on the pregnant woman and her partner.
- D. TORCH (toxoplasma, rubeola, cytomegalovirus and herpes) to the pregnant.

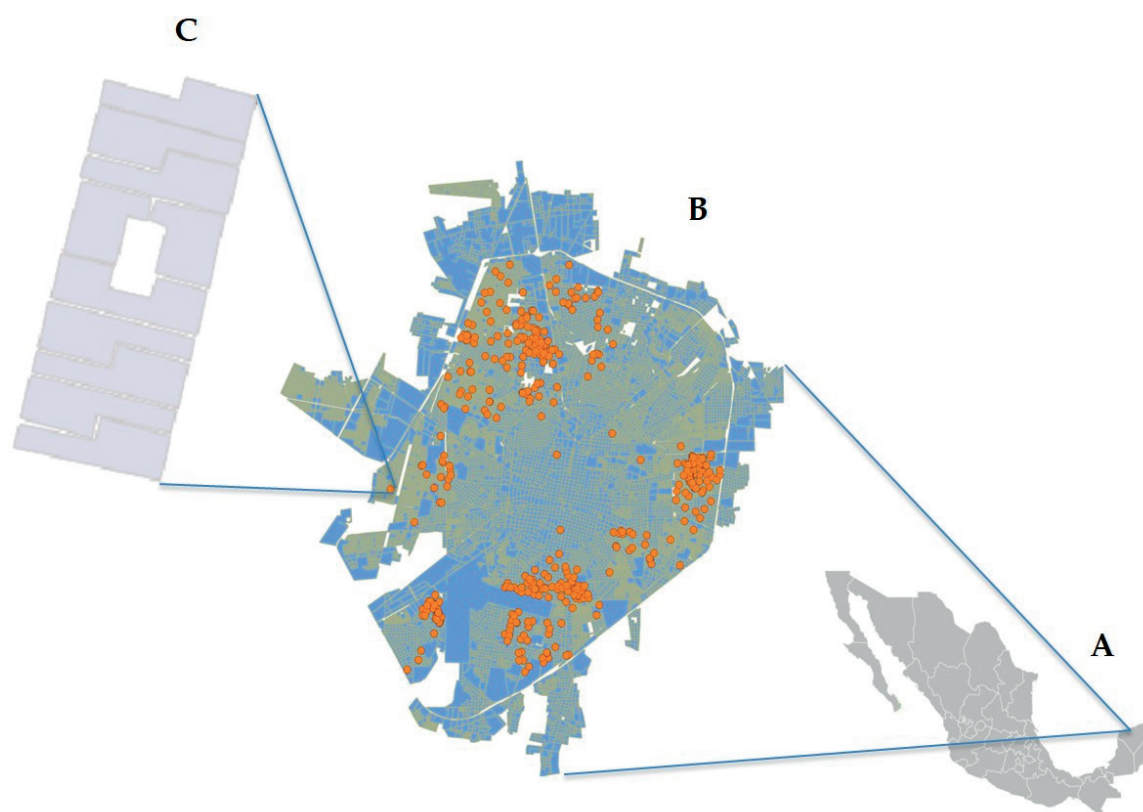


Figure 2. Map of the study areas in Merida, Yucatan, Mexico. (A) Map of Mexico with the location of the city Merida; (B) distribution of the participants of the cohort from the project families without dengue; (C) intervention area in the neighborhood Juan Pablo II.

- E. Blood count, blood chemistry, general urine test and erythrocyte folate profile in the pregnant woman.
- F. Obstetric ultrasound (quarterly).

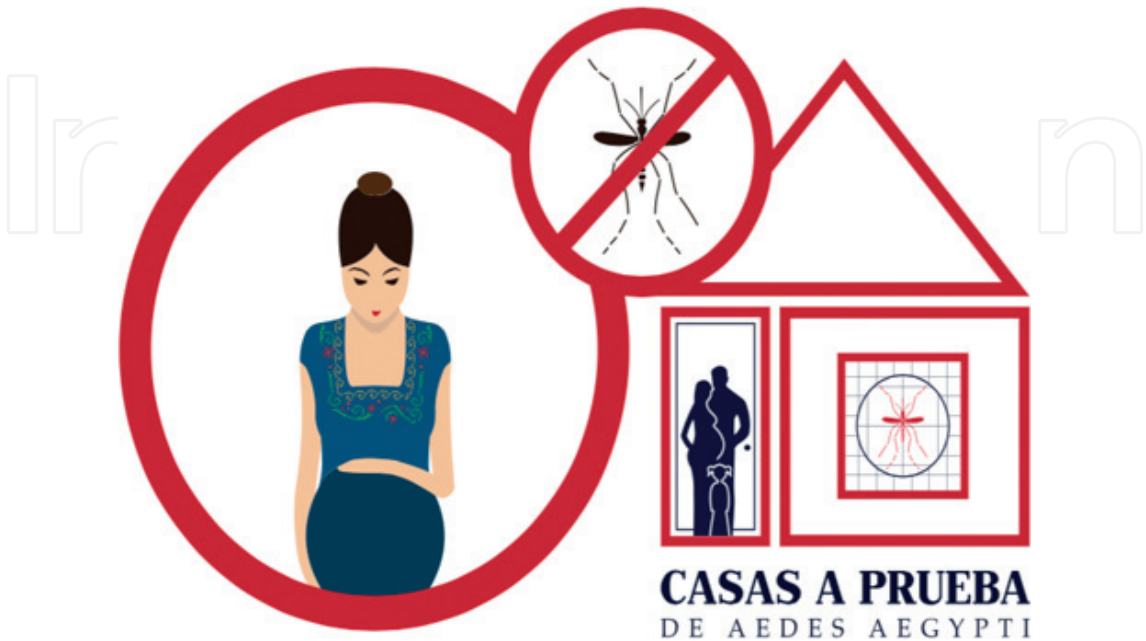


Figure 3. Identification logo of the intervention ‘Aedes aegypti-proof houses’.

In case of skin eruption, temperature of 38° or more, conjunctivitis or joint pain, please call

01800 147 9452 (01800 147 ZIKA) or to 999-738-6457

A doctor will answer to identify any related symptoms with Dengue, Chikungunya or Zika.

If necessary, an appointment will be schedule to take a blood and an urine sample.

For more information you may contact the Dr. in the Centro de Investigaciones Dr. Hileyo Niguchi Biomédicas, located in the Avenida Itzaes #400 x calle 59 or call 9 24 58 09 between 8:00 and 15:00 hrs.

INTEGRATED INTERVENTION FOR A PRIMARY AND SECONDARY PREVENTION OF THE ZIKA, DENGUE AND CHIKUNGUNYA, IN WOMEN OF REPRODUCTIVE AGE, PREGNANTS AND THEIR FAMILIES IN YUCATAN.

UADY

PRENATAL CARE REGISTRATION											
Name: _____	Date: ____/____/____		Age: _____		Folio # _____						
Size: ____ cm	Weight: ____ Kg	Gestational Age: ____ Weeks ____ Days	Probable date of birth: ____/____/____								
Pregnancies: ____ Deliveries: ____ C-sections: ____ Abortions: ____		Day of last menstrual period: ____/____/____			LMP I: ____ LMP II: ____						
Parameters:	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8	Visit 9	Visit 10	Visit 11
Date:											
Gestational Age:											
Weight:											
Blood Pressure:											
Temperature:											
Heart Rate:											
Uterine Height:											
Fetal heart rate (FHR):											
Zika in Urine:											
Folic Acid:											
Hematic Biometry:											
Blood chemistry Screen:											
Liver Function Test:											
Dm/Chik/ Zika (Blood):											
HIV Test:											
VDRL Test:											
Others:											

(a)

(b)

Figure 4. Carnet for pregnant women: (a) front cover with general information of the project and how to contact the team including a free telephonic number to communicate in case of presenting symptoms compatible with DEN/ CHIK/ ZIKV and (b) record for diagnostic tests and complementary studies that are recommended for pregnant women.

2.3. Positive cases for ZIKV

In case the participant or any member of the family has signs and symptoms compatible with DEN/CHIK/ZIKV, and have positive test result of: diagnostic test Triplex RT-PCR DEN, CHIK and ZIKV and serological tests of NS1 and IgG for dengue, IgM DEN, CHIK and ZIKV [20].

At the moment that the pregnant woman presents a positive result to ZIKV by the Trioplex RT-PCR assay for DEN, CHIK and ZIKV, she is informed of the diagnosis with counselling and psychological support in case of requesting it and the following studies and assessments are requested:

- A. Liver function tests.
- B. Structural ultrasound/obstetric ultrasound (monthly).
- C. Genetic consultation.
- D. Obstetric consultation.
- E. Amniocentesis with karyotype and diagnostic test Trioplex RT-PCR assay for DEN, CHIK and ZIKV, if required.

At the end of the pregnancy, vaginal, cesarean or abortion, biological samples will be collected to perform Trioplex RT-PCR assay for DEN, CHIK, ZIKV and anatomopathology and specialised studies (karyotype):

- A. Maternal blood
- B. Product blood
- C. Amniotic fluid
- D. Placenta
- E. Abortion product
- F. Cerebrospinal fluid

3. Implementation of communication strategies, that is, prevention and control measures against the bite of the mosquito vectors, family-planning strategies

3.1. Preventive kits

All pregnant women will be provided with an educational/preventive kit containing (**Figure 5**):

1. Proven repellent (DEET 30%) recommended by CENAPRECE (Ministry of Health) for protection outside the home.
2. Organic and environmentally friendly larvicide recommended by CENAPRECE (SPINOSAD).
3. Educational brochure for the promotion of good practices to avoid the risk of mosquito bites (including use of repellent) and for the elimination and control of Aedes breeding grounds (including the use of larvicides).
4. Thermometer for fever monitoring.

5. Personal symptom monitoring card compatible with ZIKV and Carnet for registration of laboratory tests.
6. Condoms (for prevention of possible transmission by sexual practices).
7. Access to 01800 CERO ZIKA (01800 09452) for report in case the pregnant or someone in your family presents symptoms of Zika: erythema, fever, conjunctivitis or joint pain.

To supplement these direct actions, text messages are periodically sent with information relevant to the case and reinforce preventive measures and home visits in search of febrile illnesses. Those women residing in the area where the “*Aedes aegypti*-proof houses” strategy will be evaluated will also receive the installation of long-lasting insecticide nets permanently installed in doors and windows in their homes (see more detail in the next section).

3.2. Educational intervention with women of reproductive age and their partners for the prevention of vector-borne diseases and sexually transmitted infections

The strategy of educational intervention is performed in the form of workshops. A “a pedagogical strategy, apparently simple, that by a learning methodology by doing in group, allows to build meaning to those” someone “who participate in it in order to learn and know” something “, from the integral insertion in the process” [26].

It is directed to the pregnant women who participate in the project and the women who are at reproductive age within the family nuclei. Workshops are also held with their partners so that



Figure 5. Prevention kits for pregnant women.

they are also aware of the information and are involved in the corresponding care during pregnancy. Basically, workshops deliver topics related to health, body, sexuality, pregnancy and strategies for prevention of vector-borne diseases and sexually transmitted infections.

The themes and objectives of the workshop are:

Topic 1. Body, pregnancy and sexuality.

General objective: to recognize the characteristics of the male and female body that make possible a pregnancy and the processes of a normal pregnancy, to identify the benefits of a planned pregnancy, the repercussions of an unplanned pregnancy, the health risks during pregnancy and to recognize the importance of prenatal care.

Topic 2. *Aedes*-borne diseases and the presence of ZIKV in pregnancy.

General objective: to provide information for the prevention of DEN, CHIK and ZIK, as well as the impact of this during pregnancy, identify the mechanisms of transmission:

- A. Symptoms and signs of dengue, chikungunya and Zika.
- B. Identify the activities they do and can do at home and in the community to prevent *Aedes*-borne diseases.
- C. Impact of Zika infection on pregnancy. Congenital malformations.
- D. Promotion of the use of condoms as a method of prevention of Zika.
- E. Recognize the importance of preventing Zika during pregnancy.
- F. Recognize Zika as a preventable disease and not as a determinant for the presence of congenital malformations.

Topic 3. HIV/STIs prevention.

Course objective: identify the risks of STI contagion with an emphasis on HIV.

- A. Myths and realities.
- B. Describe the most frequent STIs: HIV, gonorrhea, syphilis, herpes, and human papilloma virus.
- C. Mention what are the risk practices and routes of HIV and STI transmission.
- D. Describe clinical picture (differences between HIV/AIDS and STIs) and diagnostic methods, treatment and prognosis.
- E. Identify methods of prevention of STIs (male condom, female condom, and abstinence).

Topic 4. Protected sex.

Course objective: Provide information on the male and female condom, and promote its use.

- A. Perception of risks of contracting STIs.
- B. Myths and realities.
- C. Knowledge and importance of protected sex.

- D. Promote the practice of sex protected in sexually active population.
- E. Knowledge, characteristics and correct use of the male and female condom.
- F. Explain the correct use of the female condom (steps for its use).

Topic 5. Self-care of health.

General objective: To reflect on the self-care practices of health, identifying the consequences, and benefits of self-care.

4. Determination of the frequency of structural anomalies detected prenatally in the foetus, umbilical cord, and the placenta of pregnancies affected by infection with ZIKV

Gestation products that come to term should be evaluated for a possible congenital infection by ZIKV. Serum, placenta tissue, and urine should be obtained. The search for ZIKV RNA, immunoglobulin M and neutralizing ZIKV antibodies as well as neutralizing antibodies and M immunoglobulins for DEN is indicated. Tissue collection should be done within the first 2 days of life, if possible [11]. For this reason, all pregnancy products are evaluated by a group of experts, including clinical geneticists and pathologists, and the tissues are collected and evaluated within the first 12 hours of life. The tissues are sent to the pathology service for histopathological evaluation of the placenta and the umbilical cord. Immunohistochemical staining is performed in fixed tissue and ZIKV RNA is sought by RT-PCR in fixed and frozen tissue.

Clinical evaluation implies a dysmorphological approach and records gestational age, Apgar, occipitofrontal perimeter, height and weight. Neurological, craniofacial features, cutaneous, thoracic, and abdominal abnormalities are recorded. If a specific abnormality is observed, an evaluation by the appropriate specialist is requested [14]. Complementary studies are carried out such as transfontanellar ultrasound, auditory, and neonatal screening.

Long-term follow-up involves evaluation for 18 months and includes follow-up by geneticist, pediatrician, pediatric ophthalmology, audiology and pediatric neurology. A medical record of occipitofrontal circumference (OFC), growth, weight, height and neuromotor development is kept [16].

The possible clinical scenarios to evaluate are:

1. The patient who is observed without microcephaly or morphological alterations and has normal neurological development being the mother of a child without or with infection by ZIK and
2. Those that are observed with microcephaly, morphological alterations and / or alterations of the neuromotor development being children of mothers without or with infection or ZIKV.

In the latter group, previously well-established genetic syndromes, added teratogenic causes and/or complementary genetic studies would be ruled out according to the individual needs of each one.

The information will be collected in a database to be able to determine the frequencies.

Patients who undergo microcephaly and/or brain disruption sequence will be given skull CT and brain MRI to define CNS damage and its relationship to congenital infection by ZIKV. Other interventions will be required according to the needs of each individual [27]. Other interventions will be required according to the needs of each individual, such as the evaluation by a paediatric cardiologist in the assumption of a cardiac murmur or paediatric nephrologist for renal morphological abnormalities that compromise the function.

5. Effective vector control interventions for integrated prevention/control of *Aedes*-borne diseases (ABD) including DEN/CHIK/ZIKV and targeted on vulnerable population (pregnant women)

As described previously, the project is working to ensure that vulnerable population (pregnant women and their families) are provided with the best possible support and care, including the access of the best supplies for vector control and the prevention of *Aedes*-borne diseases (ABD); this is personal and family protection in addition to the traditional activities performed by the local health programs. This was urged in the Zika strategic response framework and joint operations plan emitted by WHO [28], commending a proactive special care for pregnant women, such as giving adequate repellent lotion and treated mosquito nets.

5.1. How can pregnant women protect themselves from mosquito bites?

The best protection from ZIKV is preventing mosquito bites. As stated by the most important agencies worldwide such as the World Health Organization [29], the CDC [30], and the Ministry of Health in Mexico, this can be done effectively and individually (and at the family level) by the integrated use of: insect repellents, the use of physical barriers such as screens on doors and windows to prevent mosquito bites outside and inside home; in an integrated manner with the elimination of mosquito breeding sites, the application of larvicides and application of insecticides to kill adult mosquitoes to control vector populations in and around homes [31].

5.2. The entomological tools and interventions selected

For an effective and integrated prevention/control of ABD in this project we have chosen: the best repellent with diethyltoluamide (DEET) available in the local market, the intervention called "*Aedes aegypti*-proof houses" ("*Casas a prueba de *Aedes aegypti**" in Spanish) which involves insecticide-treated house screening (ITS) with use long-lasting insecticidal nets (LLIN) permanently fitted to windows and doors to exclude *A. aegypti*, from houses, and the provision of an environmentally safe biorational larvicide.

5.3. Repellent

In order to select the best repellent for this project, we assessed the efficacy of commercial repellents available in Yucatan against *A. aegypti*. First results were reported by Uc-Puc et al. [32]. Protection time was determined based on WHO/CTD/WHOPES/IC and Mexican

regulations (NOM-032-SSA2-2014) [32–34]. Two products, both with DEET (N,N-diethyl-3-methylbenzamide) >25% met the recommended protection (≥ 6 hours). The best repellent was “Stop fly bung” with DEET at 30%. Efficacy was directly proportional to the concentration of DEET; botanicals repellents resulted no protective. Repellents with DEET provided more protection against *A. aegypti* and botanical repellents, including impregnated wristbands provided no protection [33, 34].

5.4. Larvicide

The selection of the larvicide was supported by previous evaluations of its efficacy under laboratory and field conditions and in consistency with the list of available products recommended by the Mexican Ministry of Health [35–38]. The product selected was the biorational and environmentally friendly larvicide Natular® DT (Spinosad 7.48%; Clarke Mosquito Control, IL, USA; WHOPES approved) which is available in the formulation of a tablet for containerized water. This product and formulation is a highly effective larvicide against *A. aegypti* with a residuality of 9 weeks in field studies. In addition is non-toxic to humans, and also an option for the management of insecticide resistance for local *A. aegypti* populations.

5.5. *Aedes aegypti*-proof houses

The intervention called *Aedes aegypti*-proof houses (“Casas a prueba de *Aedes aegypti*”) involves insecticide-treated house screening (ITS) with use long-lasting insecticidal nets (LLIN) permanently fitted to windows and doors to exclude *A. aegypti*, vector of dengue, chikungunya and Zika (Figure 6).

The selection of these interventions was based on previous studies of our group. Briefly, from 2009 to 2014, cluster randomized controlled trials were conducted in the Mexican cities of Acapulco and Merida. Intervention clusters received *Aedes aegypti*-proof houses with ITS and followed-up during 2 years. Overall, results showed significant and sustained reductions on adult vector densities in houses in the treated clusters with ITS after 2 years: ca. 50% on the presence (OR ≤ 0.62 , $P < 0.05$) and abundance (IRR ≤ 0.58 , $P < 0.05$) of indoor-resting adults. ITS



Figure 6. *Aedes aegypti*-proof houses.

on doors and windows are ‘user-friendly’ tool, with high levels of acceptance, requiring little additional work or behavioral change by householders. ITS is a housing improvement that should be part of the current paradigms for urban vector-borne disease control [36].

As described in Che-Mendoza et al. [37] and Manrique-Saide et al. [39], Duranet® screens (0.55% w.w. alpha-cypermethrin-treated non-flammable polyethylene netting [145 denier; mesh 1/4132 holes/sq. inch]; Clarke Mosquito Control, Roselle, IL, USA; WHOPES approved for LLIN use) were mounted in aluminum frames custom-fitted to doors and windows of houses in collaboration with a local small business [37, 40]. An average of two doors and five windows by house were installed in each intervention cluster. During installation, at least one person in every household received information from research staff about the proper use and maintenance of ITS.

5.6. Government agency as key partner in the intervention

These tools and interventions have fully political support by the Government of the State of Yucatán who also gave financial support. In Merida, a strong collaborative work with local authorities is already on-going and with this information we are already starting interventions (and will start others) targeting high-risk areas and vulnerable populations. The authorities of Mexico are considering how to expand *Aedes*-proof housing to as many homes as possible, probably as a targeted intervention for high-risk areas (hot-spots) of endemic localities.

6. Zika, culture and pregnancy: An anthropological overview

The particularity of Zika virus presents a ‘double identity’ because it belongs to mosquito vector-borne diseases and sexually transmitted infections. The initial cultural meanings of ZIKV produced in local population uncertainty, misinformation, social fears and rumours. Even in social networks like Facebook or Twitter, there was an entanglement of discourses that increased confusion about symptoms, treatments, and consequences of this new outbreak. Currently, we have noticed that incommensurability continues at stake on the cultural dimension of this emergent disease. That’s the reason why an anthropological overview will help us to a better understanding of the sociocultural determinants of ZIKV. The final purpose is to address cultural barriers and social acceptance of an integrated prevention model that pursuit improves population health in Yucatan.

6.1. Research process

Our group of anthropologists is currently conducting three studies as part of this integrated prevention model. First one, there is a research focused on sociocultural factors that pregnant women associated with Zika virus in Yucatan, Mexico. Ethnographic and in-deep interview methods are used for the collection data. The guidelines of this study are: source of information about ZIKV; the mechanisms associated with Zika infection; social perceptions of symptoms; cultural beliefs about microcephaly and Guillain-Barre Syndrome; risk perceptions on Zika virus; and the prevention and control practices of this target population. Also, we make

anthropological analysis on focus group and workshops activities developed by medical crew with pregnant women.

Second, there is research which main goal is focused on human mobility and its relation with DENV, CHIKV and ZIKV transmission in Yucatan. A former and pioneer study was deployed in Iquitos, Peru since 2007 [40]. We adapted surveys applied there to Yucatecan context, coordinated by Gonzalo Vazquez-Prokopec. There are two types of questionnaires: the retrospective movement survey and the prospective movement survey. The first one, will help to identify the amount of time DEN/CHIK/ZIKV-infected person spends at home as well array locations. The second one is for not infected individuals. In both cases, we want to know about their routine movements and the time-spatial quantification of them.

Third, we are making a rapid assessment on social perception about insecticide-treated screening (*Aedes aegypti*-proof houses). Pregnant women and their families are the main target of this study. The topics this survey are: acceptance of the intervention, installation process, family perception on positive and negative impacts of this technological innovation, comfort and heat perception, families' opinion on scale-up this project.

Finally, we are conducting a sociological assessment on the integrative prevention model. We seek to address what is the social perception of pregnant women about the intervention (enrollment process, information of Zika and ABD prevention practices), and follow-up health care of pregnancy). In addition, we are exploring with in-deep interviews vulnerability experiences that pregnant women have lived during and after the emergence of Zika outbreak in Yucatan.

6.2. Anthropological contributions

We expect, that this three and incoming social studies, will provide cross-cultural perspectives on entomological, medical, ecological and epidemiological approaches. The common goal to achieve, as a multidisciplinary team, is to produce a very positive impact of named interventions in collaboration with local communities and government institutions. Since anthropological point of view, we are strengthening the integrated prevention model by studying how human factor is interweaved in an eco-bio-social context.

7. Discussion and conclusions

Here we described and discussed the design and current implementation of an integrated model for primary and secondary preventive interventions for ZIKV, along with other ABD and sexually transmitted infections that impact reproductive health, pregnancy and perinatal life stages in women and their upspring in Merida, Mexico.

This intervention is being developed in a population of 10,000 people of the city of Merida and with the participation of a multidisciplinary group of public health professionals (epidemiologists, obstetricians, geneticists, virologists, immunologists, pathologists, entomologists, ecologists, sexologists and anthropologists), in collaboration with the Ministry of Health and the Government of Yucatan.

There is not a full understanding of the risk for pregnant women, and the teratogenicity of prenatal infections with ZIKV has not been completely elucidated [7, 10, 11, 13–15]. It is urgent that a protocol designed for surveillance of pregnant women in endemic and invasive zones of *A. aegypti* allow collection of information about the effects of ZIK in pregnant women, and to delineate the neonatal phenotype of congenital abnormalities of the fetus related with ZIK. This protocol will allow the establishment strategies related to the prevention and control of emerging infectious diseases for future use [41, 42].

The implementation of complementary, innovative (not included by the traditional vector control programs), feasible and locally adapted approaches to vector control to reduce the risk of Zika and other ABD, through personal protection, environmental management and community-based partnership models can improve the current strategies for ABD prevention and control.

The results from the surveillance in a vulnerable population, will enable at least four strategies: (1) create a program focused on a rapid recognition of any clinical symptoms for ZIKV; (2) set up rehabilitation programs for motor, hearing and visual disabilities in order to support neurodevelopment and quality of life for patients; (3) determine the performance of current vector control and (4) establish measures and protocols in accordance with each specific population to ensure the best results in surveillance, prevention and control of vector-borne diseases in vulnerable populations. Finally, this strategy will allow development of human resources in research, including educational cooperation and special experience in handling patients affected by ZIKV.

Therefore, this proposal will have direct impact on social, educational, economic and environmental aspects concerned with the general health of the population, the collaboration and engagement with government institutions are key factors to accomplish common goals on public health and preventive strategies against vector-borne diseases.

Acknowledgements

The studies are funded by the Office of Infectious Disease, Bureau for Global Health, U.S. Agency for International Development, under the terms of an Interagency Agreement with CDC. The opinions expressed herein are those of the author(s) and do not necessarily reflect the views of the U.S. Agency for International Development. It is also financed by Sanofi Pasteur Sanofi Pasteur INC, Special Programme for Research and Training in Tropical Diseases (TDR) at the World Health Organization in a partnership with the Ecosystem and Human Health Program of the International Development Research Centre (IDRC) of Canada within the program “Towards Improved Dengue and Chagas Disease Control through Innovative Ecosystem Management and Community-Directed Interventions: An Eco-Bio-Social Research Programme on Dengue and Chagas Disease in Latin America and the Caribbean” (Project 104951-001) and the Canadian Institutes of Health Research (CIHR) and IDRC (Preventing Zika disease with novel vector control approaches Project 108412). The nets, repellent and larvicide employed in this study were donated by the company Public Health Supply and Equipment de Mexico, S.A. de C.V. The nets and larvicide and repellent employed in this study were donated by the company Public Health Supply and Equipment de Mexico, S.A. de C.V.

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