INVESTIGATION PROJECT

COHORT OF PREGNANT WOMEN WITH RASH IN THE STATE OF PERNAMBUCO

(MICROCEPHALY EPIDEMIC RESEARCH GROUP – MERG

RECIFE

2016

COHORT OF PREGNANT WOMEN WITH RASH IN THE STATE OF PERNAMBUCO

PURPOSES:

To estimate the frequency of microcephaly and other abnormalities of the central nervous system and other malformations in newborns of pregnant women showing rash, in accordance with the gestational age at which the rash occurred.

To estimate frequencies abovementioned separately for women with serological and molecular diagnosis of Zika virus, for those with other diagnoses and those without serological and molecular diagnosis.

To identify other adverse outcomes most frequent in neonates of pregnant women with rash compared to pregnant women without rash, including other malformations and occurrence of miscarriage.

To verify the incidence of seroconversion or rash in the cohort without rash incidence as indication of infection by ZikaV in the population.

STUDY DESIGN

Prospective study of two cohorts of pregnant women, one of pregnant women presenting rash and one of pregnant women not presenting rash.

STUDY POPULATION AND PLACE

Pregnant women residing in the metropolitan region of Recife. Two cohorts of pregnant women defined according to the presence or absence of rash will be recruited.

Cohort of pregnant women recruited with rash

Pregnant women with rash independent of the gestational age and rash characteristics will be recruited, who will be followed until the end of pregnancy. Only pregnant women who are still presenting rash will be included, not fitting in these criteria those reporting this change, even if the report is of a recent episode.

Cohort of pregnant women without rash

Pregnant women in the first trimester will be included, followed until the appearance of rash or until the end of pregnancy.

Note 1: In case these women present rash, they will be transferred to the other cohort.

Note 2: In case these women present no rash, but have a ZikaV infection diagnosis (virus identification by PCR), they will be considered a separate group. If the number of

women in this group is appropriate, newborns of these pregnant women will be compared with those born to women with rash, to see if the frequency of microcephaly and other abnormalities differ in both groups.

RECRUITING THE COHORTS

Pregnant women with rash (n = 500) will be recruited from the notification to the State Health Department of Pernambuco, through the Cievs platform, through FormSUS available at the website: cievspe.com or from attendance to health services responsible for the greatest number of notifications (60% of notifications): Hospital João Murilo and Policlínica de Vitória, Instituto de Medicina Integral Prof. Fernanndo Figueira, Centro Integrado de Sáude Amauri de Medeiros, Hospital Agamenon Magalhães, Hospital Barão de Lucena, Maternidade Bandeira Filho.

At these places, identification data will be collected, the questionnaire will be applied and collection of blood and urine and subsequent examinations will be performed.

Pregnant women without rash (n = 200) will be recruited prenatally in the same units that notify pregnant women with rash.

INFORMATION COLLECTION

A standardized questionnaire to characterize the rash and the underlying clinical condition will be applied. The rash will be characterized regarding the time of onset, location and duration, seeking to identify the one most commonly presented by patients with infection by Zika virus. The underlying worsening will be characterized regarding the presence and intensity of fever, joint involvement: pain - presence and intensity - and edema, itching, headache report, presence of conjunctivitis and lymphatic hypertrophy. Photographic documentation of the rash will be made.

To identify the infectious etiology, blood collection for investigation - IgG and IgM - of Zika virus, Chikungunya, dengue, cytomegalovirus, rubella, toxoplasmosis and parvovirus B19 will be performed. Blood samples (serum) will be collected until the 5th day of the onset of symptoms and urine until the 8th day, in accordance with the Clinical and Epidemiological Protocol for Microcephaly of Pernambuco's State Health Department. A second blood sample (serum) will be collected with an interval of 14 and 21 days after the first one, at the health service of prenatal care. Samples of blood and urine will also be tested by PCR to identify Zika virus, Chikungunya, Dengue, Toxoplasmosis and Cytomegalovirus. For pregnant women without rash, a second collection at the end of pregnancy or at delivery will be performed.

Serology will be performed at LACEN, except for Zika virus, that will be held at Fiocruz - PE. Molecular biology exams for Chikungunya, Dengue, Toxoplasmosis and Cytomegalovirus will be performed at LACEN, and Zika virus at Fiocruz - PE.

To determine the gestational age and for later identification of fetal abnormalities, two ultrasounds will be performed, in the first and last trimester of pregnancy (between the 32nd and 35th week of pregnancy) as provided for in the Protocol of the State Health Department. For pregnant women without rash, only one ultrasound as routine follow-up will be performed.

For identification and description of malformations of newborns with and without microcephaly, born from the cohort of pregnant women with rash, the same clinical investigation protocol of the case-control study will be applied. For identification of malformations of newborns born from pregnant women in the cohort without rash, a detailed medical investigation will be held.

DATA ENTRY

It will be prepared a platform that includes a structured database; masks for data collection in tablet, with mechanisms for automatic data entry.

ANALYSIS PLAN

In the cohort of pregnant women with rash, the frequency of the following outcomes will be verified: microcephaly, cerebral calcifications in the absence of microcephaly, other abnormalities of the central nervous system development, other malformations, fetal loss, prematurity, and fetal deaths.

The association of gestational age is checked at the time of onset of the rash with the Zika virus diagnosis with microcephaly development or other abnormalities of the central nervous system in the newborn will be verified.

In the cohort with rash, the interaction between positive serology for dengue and rash suggestive of ZikaV or laboratory confirmation of the presence of ZikaV and microcephaly and other malformations will be verified.

In the cohort of pregnant women without rash, the frequency of the following outcomes will be verified: incidence of rash, fetal loss, pre-term birth, malformations and fetal deaths.