

## Dengue infection during pregnancy and adverse maternal, fetal, and infant health outcomes in Rio Branco, Acre State, Brazil, 2007-2012

Os efeitos maternos, fetais e infantis decorrentes da infecção por dengue durante a gestação em Rio Branco, Acre, Brasil, 2007-2012

Los efectos maternos, fetales e infantiles derivados de la infección por dengue durante la gestación en Río Branco, Acre, Brasil, 2007-2012

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### Abstract

*The effects of dengue infection during pregnancy have not been previously studied in Rio Branco, Acre State, Brazil. The aim of this study was to determine the risks of maternal, fetal, and infant complications resulting from dengue infection during pregnancy. The study compared two cohorts of pregnant women, exposed versus unexposed to dengue virus, from 2007 to 2012. Incidence rates and risk ratios were estimated for maternal, fetal, and infant complications. In the exposed cohort there were 3 fetal deaths and 5 neonatal deaths. Two maternal deaths were identified in the exposed cohort, as opposed to none in the unexposed group ( $p = 0.040$ ). The exposed cohort showed a risk ratio (RR) of 3.4 (95%CI: 1.02-11.23) for neonatal death. The risk ratio for early neonatal death was 6.8 (95%CI: 1.61-28.75). Ten infant deaths occurred in children of exposed pregnant women and 7 in unexposed (RR = 6.0; 95%CI: 2.24-15.87). Women infected with dengue virus in pregnancy showed increased risk ratio for maternal, neonatal, and infant mortality.*

*Dengue; Pregnancy; Maternal Mortality; Infant Mortality*

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## Introduction

Considered one of the most important arbovirus infections in humans, dengue is a serious international public health problem, especially in tropical countries, where environmental conditions favor the development and proliferation of *Aedes aegypti*, principal mosquito vector of the disease. Some 40% of the world's population is at risk of acquiring the disease, in more than 100 endemic countries. Dengue is caused by four viral serotypes (DENV-1, DENV-2, DENV-3, and DENV-4), which can succeed each other, circulating in populations, or even coexist. The World Health Organization (WHOS) estimates approximately 50 to 100 million cases of dengue per year worldwide <sup>1,2</sup>.

In the State of Acre, Brazil, dengue transmission has occurred since the year 2000. The first autochthonous cases were detected in Rio Branco, the state capital. The first epidemic occurred in the year 2001, when serotypes DENV-1 and DENV-2 were identified. The second epidemic occurred in the year 2004 with the introduction of serotype DENV-3. New epidemics occurred in the years 2009 (DENV-2), 2010 (DENV-1, 2, and 3), and 2011 (DENV-1 and 3), while in 2010 the State of Acre witnessed one of its worst epidemics, with 37,098 reported cases and an incidence of 11,039.82/100,000 inhabitants. The year 2012 saw laboratory confirmation of circulation of DENV-4 in Rio Branco.

Lack of infrastructure in cities, the urbanization process, and population habits are factors contributing to the spread of the disease, creating favorable ecological conditions for the increase in the number of cases and the occurrence of epidemics, which are becoming increasingly frequent, with epidemic peaks every 3-5 years <sup>3,4</sup>. Brazil's climatic and socioeconomic conditions, favorable to spread of the disease, disordered population growth, and lack of basic sanitation allow the expansion of the disease <sup>3</sup>.

In Brazil, since the introduction of the virus, young adults have been hit most heavily by the disease. However, the more recent epidemics have shown a rise in the number of cases in adult women and preschool children. This changing trend in dengue's epidemiological profile, especially in the context of epidemics, can increase the risk of dengue virus infection in pregnant women <sup>5</sup>.

The natural physiological process of maternal immune suppression in pregnancy may favor the occurrence of more serious infections and consequently greater fetal susceptibility to congenital infections, potentially harming the health of both the mother and fetus <sup>2,6,7,8</sup>.

When acquired during pregnancy, viral infections make pregnant women more prone to complications and are considered the principal causes of fetal morbidity and mortality <sup>9,10</sup>. There are viruses like rubella, cytomegalovirus, hepatitis, and HIV for which scientific knowledge exists on the impact for maternal and fetal health. However, the implications of dengue for pregnancy outcomes have not been completely elucidated, so that knowledge on this issue is still insufficient and controversial <sup>8,11,12,13,14</sup>.

Some studies have reported that severe dengue during pregnancy is associated with maternal, fetal, and neonatal deaths. Other unfavorable outcomes have also been described, such as low birth weight, premature birth, miscarriage, fetal distress, and vertical transmission <sup>8,12,14,15,16</sup>.

The aim of this study was to determine the magnitude of risks of maternal, fetal, and infant complications from dengue infection during pregnancy in Rio Branco from 2007 to 2012.

## Material and method

### Study design

This was a retrospective cohort study in Rio Branco, capital of the State of Acre, from 2007 to 2012.

### Study population

The study population consisted of women residing in the city of Rio Branco with pregnancies outcomes recorded from 2007 to 2012, and their respective offspring. Two hundred pregnant women were identified who had been exposed to dengue virus in pregnancy during this period, and the distri-

bution of the selected pregnancy outcomes was compared to that in a sample of 800 pregnant women unexposed to dengue during pregnancy.

### **Selection of the exposed population**

The exposed cohort consisted of pregnant women reported as dengue cases in the Brazilian Information System for Notifiable Diseases (SINAN) from 2007 to 2012, confirmed by laboratory criterion (positive IgM serology for dengue) or clinical/epidemiological criterion. A total of 388 pregnant women were identified who met the criteria. However, to be eligible for the study, these pregnant women had to be identified as the mothers in the Brazilian Information System on Live Births (SINASC) or the Brazilian Mortality Information System (SIM); 197 were identified in SINASC and 3 in SIM, totaling 200 pregnant women in the exposed cohort. One hundred and eighty-eight purportedly pregnant women were not located in either the SINASC or SIM database.

### **Selection of the unexposed population**

The pregnant women in the unexposed cohort were selected from the SINASC database by simple random sampling, considering a proportion of 4 unexposed pregnant women for each exposed pregnant woman, matched according to their year of birth and neighborhood, with 800 pregnant women in the final selection. Before selection of the unexposed cohort, all the pregnant women selected for the exposed cohort were excluded from the SINASC database.

### **Data collection**

The data were made available by the Rio Branco Municipal Health Secretariat (SEMSA), through the Division of Information and Data Analysis (DIAD) of the Department of Epidemiological and Environmental Surveillance (DVEA).

Data on dengue in SINAN allowed obtaining the first variables for organization of the database, subsequently complimented by information from SINASC and/or SIM. The database was developed by probabilistic record linkage of these systems (SINAN, SINASC, and SIM), in which the mother's name was used as the key field, such that the similar (but not identical) mothers' names were verified manually with other personal data to confirm whether the different names belonged to different persons. After the data check, the database organized was in a database management system (DBMS) Access 2013, version 15.0.4569.1503 (Microsoft Corp., USA). Data were normalized and displayed in tables for use in research methods in Structured Query Language (SQL).

### **Data analysis**

Linkage of SINAN and SINASC allowed verifying the type of pregnancy and type of delivery, as well as the occurrence of low birth weight, prematurity, and 1-minute and 5-minute Apgar scores. The SIM was also explored for maternal, fetal, neonatal, and infant deaths.

Absolute and relative frequencies were calculated for each of the selected variables, with the proportions compared using Pearson's chi-square or Fisher's exact test, and the means or medians by student's t-test or Mann-Whitney test, when applicable, with significance set at 5%. Subsequently, incidence rates were calculated for the outcomes in each cohort and the risk ratios (RR) were obtained with their respective 95% confidence intervals (95%CI) for each of the target outcomes.

The data were analyzed with IBM SPSS 20.0 (IBM Corp., Armonk, USA).

## Results

During the study period (2007 to 2012), 94,790 suspected cases of dengue were reported in Rio Branco. Of the 50,065 notifications (52.8%) in females, 37,139 (74.2%) occurred in women from 10 to 49 years old, considered childbearing age.

During the year 2007, 306 dengue cases were confirmed, of which 301 by the laboratory criterion and 5 by the clinical/epidemiological criterion. In 2008 there were 1,651 cases, of which 51.4% confirmed by the laboratory criterion; in 2009 there were 17,149 cases and 10.6%; in 2010, 32,437 cases and 9.2%; in 2011, 17,998 cases and 11%; and finally in 2012, 1,745 and 59% with laboratory confirmation. Rio Branco suffered an intense dengue epidemic from 2009 to 2012.

From 2007 to 2012, 543 cases of dengue in pregnant women were reported, of which 71.5% (388) were confirmed, 80.2% (311) by the clinical/epidemiological criterion and only 19.9% (77) by laboratory (Figure 1). As for annual distribution of cases, ninety percent of the cases reported in pregnant women from 2007 to 2012 occurred in the 2009-2011 three-year period, during the above-mentioned epidemic in Rio Branco.

Pregnant women from the exposed cohort showed a mean age of 24.78 years, ranging from 14 to 44, while mean age in the unexposed cohort was 24.83 years ( $p = 0.739$ ).

Distribution by trimester of pregnancy in which the dengue occurred was relatively homogeneous: 28.2% of cases in the 1<sup>st</sup>, 30.3% in the 2<sup>nd</sup>, and 41.5% in the 3<sup>rd</sup> trimester.

The two study cohorts showed similar profiles, as shown in Table 1. The largest proportion of women were in the 20-29 year age bracket ( $p = 0.225$ ). More than 70% had a university education ( $p = 0.157$ ), the majority of the women were married ( $p = 0.719$ ), and there was a high percentage of women with brown skin color ( $p = 0.591$ ). As for type of pregnancy, there were only 5 cases of twin pregnancies ( $p = 0.589$ ). Cesarean rate was 41.7% in the exposed cohort versus 42.8% in the unexposed cohort ( $p = 0.790$ ).

The two groups showed similar distributions of the newborns' sex, with 51.8% males in the exposed cohort versus 51% in the unexposed cohort ( $p = 0.848$ ).

Median 1-minute Apgar was 8 and median 5-minute Apgar was 9 in both cohorts. Mean birth weight in the exposed cohort was 3208.65g versus 3225.19g in the unexposed cohort ( $p = 0.264$ ). The exposed cohort showed a mean gestational age at birth of 39.3 weeks, and the unexposed cohort showed a mean of 38.8 weeks ( $p = 0.135$ ). There were 18 cases (9%) of infants with low birth weight, defined as  $< 2500$ g, in the exposed and 61 (7.6%) in the unexposed cohort, with a risk ratio of 1.2 (95%CI: 0.69-2.09). Prematurity, defined as gestational age  $< 37$  weeks, was identified in 2.9% of the exposed cohort and 4.3% of the unexposed cohort (RR = 0.7; 95%CI: 0.20-2.18). Low 1 and 5-minute Apgar scores (asphyxia), defined as  $< 7$ , did not present significant associations, as shown in Table 2.

Neonatal mortality was higher in the exposed cohort, such that children of mothers exposed to dengue virus during pregnancy showed 3 times higher risk (RR = 3.4; 95%CI: 1.02-11.23) of dying in the first 28 days of life. This risk ratio increases when analyzing only the deaths that occurred in the early neonatal period, defined as deaths in the first 7 days of life (RR = 6.8; 95%CI: 1.61-28.75). The same was true for infant deaths, with a 6-fold risk in the exposed cohort (RR = 6.0; 95%CI: 2.24-15.87) for death in the first year of life. The infant mortality rate in the exposed cohort during the study period was 50.8/1,000 live births.

There were 2 maternal deaths in the exposed cohort, one of which directly related to dengue. No maternal deaths occurred in the unexposed cohort ( $p = 0.040$ ). The maternal mortality ratio in the exposed cohort was 1.015/100,000 live births.

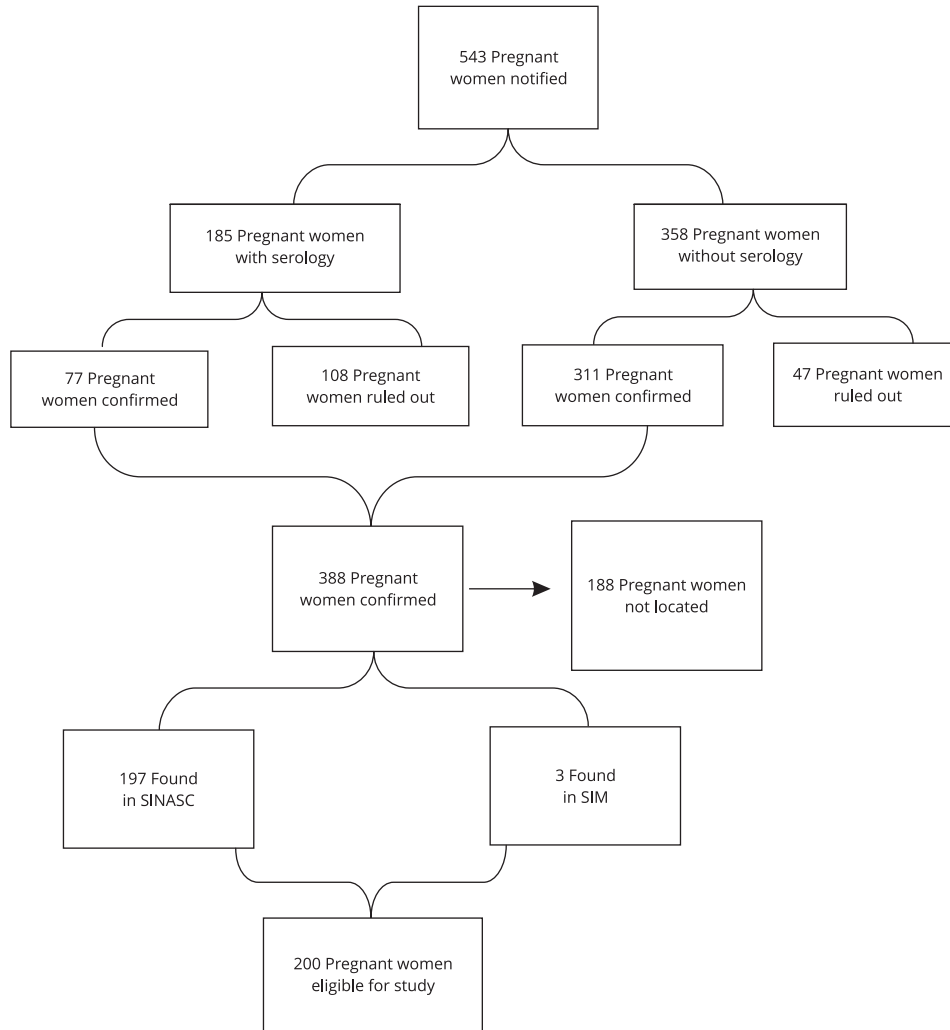
The perinatal mortality rate in the exposed cohort was 4% (defined as the sum of fetal deaths plus early neonatal deaths), with 1.5% of fetal deaths. The fetal mortality rate in the exposed cohort during the period was 15/1,000 live births.

## Discussion

During the study period, according to data from the SINAN, there were 388 confirmed cases of dengue in pregnant women in Rio Branco. However, after linking this system and SINASC and

**Figure 1**

Database linkage for pregnant women with confirmed dengue, Brazilian Information System for Notifiable Diseases, Brazilian Information System on Live Births (SINASC) and Brazilian Mortality Information System (SIM) databases, Rio Branco Municipal Health Secretariat, Acre State, Brazil, 2007-2012.



Sources: Brazilian Information System on Live Births and Brazilian Mortality Information System (DATASUS, <http://www.datasus.gov.br>). Rio Branco Municipal Health Secretariat, 2013 (<http://www.saude.ac.gov.br/wps/portal/saude/saude/principal/>).

SIM, only 200 cases were identified, and the information for 188 was not located in any of these systems after the database linkage. For this subset of cases, we attempted to retrieve the information by telephone contact, revealing that some of these women were erroneously notified in the SINAN database as pregnant ( $n = 46$ , 24.5%), but it was not possible to establish contact with all the women not located. Therefore, another possible hypothesis is miscarriage, which was not available in the above-mentioned databases.

**Table 1**

PSocio-demographic and obstetric characteristics of pregnant women exposed versus unexposed to dengue virus in Rio Branco, Acre State, Brazil, 2007-2012.

Characteristic	Exposed cohort [n = 200] n (%)	Unexposed cohort [n = 800] n (%)	p-value
Age (years)			0.225
10-19	37 (18.5)	178 (22.2)	
20-29	124 (62.0)	442 (55.3)	
30-39	33 (16.5)	164 (20.5)	
40-49	6 (3.0)	16 (2.0)	
Schooling			0.157
Primary	20 (10.1)	49 (6.2)	
Secondary	37 (18.6)	151 (19.0)	
University	141 (71.3)	596 (74.8)	
Marital status			0.719
Single	42 (21.5)	180 (22.6)	
Married	153 (78.5)	613 (76.8)	
Widow	-	1 (0.1)	
Divorced	-	4 (0.5)	
Skin color			0.591
White	10 (15.2)	29 (14.4)	
Black	3 (4.5)	3 (1.5)	
Brown	53 (80.3)	169 (83.6)	
Indigenous	-	1 (0.5)	
Type of pregnancy			0.589 *
Singleton	199 (100.0)	795 (99.4)	
Twins	-	5 (0.6)	
Type of delivery			0.790
Vaginal	116 (58.3)	458 (57.2)	
Cesarean	83 (41.7)	342 (42.8)	

Sources: Brazilian Information System on Live Births and Brazilian Mortality Information System (DATASUS, <http://www.datasus.gov.br>).

Rio Branco Municipal Health Secretariat, 2013 (<http://www.saude.ac.gov.br/wps/portal/saude/saude/principal/>).

\* Fisher's exact test.

Mean age of the mothers exposed to dengue virus in pregnancy in Rio Branco was 24.8 years, similar to the mean age in a cohort study in Rio de Janeiro <sup>17</sup> and lower than in French Guiana <sup>18</sup> and Malaysia <sup>15</sup>.

Dengue cases showed uniform distribution according to the trimester in which the infection occurred, with a slight increase in the number of cases in the 3<sup>rd</sup> trimester, similar to a previous study in Colombia <sup>19</sup>. In another study, dengue infections were more frequent in the 1<sup>st</sup> trimester of pregnancy (45.4%) <sup>13</sup>. Carles et al. <sup>20</sup> in French Guiana found a higher rate of infection in the 2<sup>nd</sup> trimester (40.9%). The trimester in which dengue infection occurs apparently affects the rate of adverse outcomes, so that mothers infected in the first trimester have a higher risk of fetal death <sup>14,21</sup>. However, when the infection occurs in the third trimester, the risks increase for low birth weight, premature labor, and vertical transmission <sup>16,17,21,22</sup>.

Of the 200 pregnant women in the exposed cohort in this study, 23% were confirmed by the laboratory criterion and 77% by the clinical/epidemiological criterion. The high number of notifications in the epidemic years may have hindered serological testing to confirm the cases in the laboratory. However, the percentage of cases confirmed by laboratory exceeded the 10% recommended by the

**Table 2**

Low birth weight, prematurity, 1 and 5-minute Apgar score, and neonatal and infant deaths in the cohorts exposed and unexposed to dengue virus in pregnancy in Rio Branco, Acre State, Brazil, 2007-2012.

Characteristic	Exposed cohort n (%)	Unexposed cohort n (%)	RR (95%CI)
Low birth weight			1.2 (0.69-2.09)
< 2500g	18 (9.0)	61 (7.6)	
≥ 2500g	181 (91.0)	739 (92.4)	0.7 (0.20-2.18)
Prematurity (weeks)			
< 37	3 (2.9)	33 (4.3)	
≥ 37	102 (97.1)	737 (95.7)	
1-minute Apgar			1.5 (0.63-3.68)
< 7	7 (3.9)	19 (2.6)	
≥ 7	174 (96.1)	719 (94.4)	
5-minute Apgar			2.7 (0.45-16.50)
< 7	2 (1.1)	3 (0.4)	
≥ 7	179 (98.9)	735 (99.6)	
Neonatal death	5 (2.5)	6 (0.8)	3.4 (1.02-11.23)
Early neonatal death	5 (2.5)	3 (0.4)	6.8 (1.61-28.75)
Infant death	10 (5.0)	7 (0.9)	6.0 (2.24-15.87)

95%CI: 95% confidence interval; RR: risk ratios.

Sources: Brazilian Information System on Live Births and Brazilian Mortality Information System (DATASUS, <http://www.datasus.gov.br>). Rio Branco Municipal Health Secretariat, 2013 (<http://www.saude.ac.gov.br/wps/portal/saude/saude/principal/>).

Ministry of Health in epidemic periods<sup>3</sup>. Meanwhile, in Colombia the opposite situation was found in two studies, in which 71% and 72.7% of mothers showed IgM-positive serology<sup>13,23</sup>.

Some studies have reported a higher cesarean rate in pregnant women with dengue, ranging from 50% to 53.8%<sup>11,17</sup>, higher than the rate in the current study (41.7%).

According to the current study, low birth weight did not differ significantly when comparing newborns of exposed versus unexposed mothers ( $p = 0.264$ ), contrary to a study by Restrepo et al, in which low birth weight was associated with maternal exposure to dengue ( $p = 0.045$ )<sup>13</sup>. The association between maternal exposure to dengue in pregnancy and low birth weight should be analyzed with caution, since prematurity and other maternal conditions may be associated with low birth weight. In some studies, other variables were associated with low birth weight in which maternal exposure to dengue virus occurred, such as prematurity, smoking in pregnancy, and maternal hypertension<sup>13,14,17</sup>.

The premature birth rates were 2.9% in the exposed cohort and 4.3% in the unexposed cohort, so that exposure to dengue virus in pregnancy showed an inverse association with prematurity in this population, but without statistical significance, corroborating Restrepo et al.<sup>13,19,23</sup>. Contrary to this result, Carles et al.<sup>22</sup> reported a twofold risk of premature birth in the exposed group when compared to the overall population of pregnant women ( $p < 0.05$ ), and the same was true in Rio de Janeiro, Brazil, with 53.8% prematurity in a series of 13 pregnant women exposed to dengue<sup>17</sup>. Another important finding in the literature was the high rate of premature labor without delivery, occurring in 50% of the women in studies in Malaysia<sup>15</sup> and 55% in French Guiana<sup>22</sup>. In Cuba, a study reported 3.7 times higher risk of this event<sup>24</sup>.

The 1-minute Apgar score did not show statistically significant differences. However, according to the 5-minute Apgar, although not statistically significant, maternal exposure to dengue increased the risk of asphyxia at five minutes after birth. In 2 consecutive studies in Colombia, asphyxia at 5 minutes was significantly higher in newborns of mothers exposed to dengue<sup>13,19</sup>.

Since 2007, Rio Branco has shown a drop in infant mortality, from 21 deaths per 1,000 live births to 12.6/1,000 live births in 2012 (Brazilian Health Informatics Department. DATASUS. <http://www2>).

datasus.gov.br/DATASUS/index.php?area=0205, accessed on may/2017). The infant mortality rate in the exposed cohort during the study period was 50.8/1,000 live births, nearly four times higher than the rate in the overall population in 2012.

There were 2 maternal deaths (1%) in the exposed cohort and none in the unexposed cohort ( $p = 0.040$ ). Of the two maternal deaths, one was directly related to dengue virus infection. The maternal mortality ratio in the exposed cohort was 1,015/100,000 live births, or 13 times the mean maternal mortality ratio in Rio Branco from 2009 to 2012, which was 76.27/100,000 live births (Brazilian Health Informatics Department. DATASUS. <http://www2.datasus.gov.br/DATASUS/index.php?area=0205>, accessed on May/2017). Maternal deaths in various studies have been associated with severe dengue. Ismail et al.<sup>15</sup> reported 3 maternal deaths in a series of 16 women exposed to dengue in pregnancy, associated with clinical evolution to dengue shock syndrome. Of 78 pregnant women with dengue in Sudan, 17 (21.7%) evolved to maternal death due to hemorrhage<sup>25</sup>. In Rio de Janeiro, 2 maternal deaths were reported in 13 pregnant women exposed to dengue<sup>17</sup>. In a study of 53 pregnant women exposed to dengue, Basurko et al.<sup>18</sup> identified a maternal case-fatality rate of 1.9%. In Colombia, a study showed 2.6% maternal deaths in the exposed cohort and no deaths in the group of pregnant women not exposed to dengue<sup>19</sup>.

According to a study in Rio de Janeiro by Machado et al.<sup>26</sup>, pregnant women were 3.4 times more likely to develop severe dengue (OR = 3.38; 95%CI: 2.10-5.42), and mortality was higher in pregnant than in non-pregnant women. Therefore, any pregnant woman with an acute febrile illness, especially in endemic areas, should be investigated for dengue virus infection, since the increased probability of evolution to the severe form during pregnancy requires closer surveillance of pregnant women infected with the virus<sup>27</sup>.

The exposed cohort showed a 1.5% fetal mortality rate. Maternal dengue has been associated with fetal death, especially in severe infections or infections in the first trimester of pregnancy. Plasma leakage that occurs in cases of severe dengue can compromise fetal-placental circulation and lead to fetal death<sup>14</sup>. Ismail et al.<sup>15</sup> reported 1 in-utero fetal death related to dengue hemorrhagic fever among 16 pregnant women in Malaysia. In French Guiana, 3 fetal deaths were reported among 22 pregnant women<sup>20</sup>. In 2009, in French Guiana Basurko et al.<sup>18</sup> found a 3.8% in-utero fetal death rate among 53 pregnant women exposed to dengue virus (DENV-1), and a case series in Rio de Janeiro found a 7.7% rate<sup>17</sup>.

The fetal mortality rate in exposed cohort was 15/1,000 live births, twice as high as the mean fetal mortality rate in Rio Branco, which was 7.3/1,000 live births in the last 5 years. The rate in the exposed cohort in this study was well below the rate of 131.5/1,000 live births in French Guiana<sup>22</sup>.

It was only possible to calculate the perinatal mortality rate in the exposed cohort (4%), since the incidence rates for fetal deaths and perinatal deaths were not verified in the unexposed cohort, because the latter group consisted only of mothers of infants recorded in the SINASC.

In the exposed cohort, we identified 5 neonatal deaths (2.5%), all in the first 7 days of life, i.e., classified as early neonatal deaths. The case series in Malaysia included 1 early neonatal death (6.3%)<sup>15</sup>, and in French Guiana there were 2.6% neonatal deaths in 38 pregnant women with dengue<sup>22</sup>.

The current study, on exposure to the dengue virus in pregnancy, conducted with a cohort design and database linkage, allowed analyzing a larger sample than in previous studies on this topic, and the results showed more robust associations than those reported in the literature.

The study's limitations mainly involve the use of retrospective secondary data. Although such studies based on health information systems may suffer limitations related to the use of these data, one important advantage is that they allow population-based studies with a nationwide scope and at low cost. Based on appropriate questions and acknowledging the potentialities and limitations of health information systems, such studies allow new ways of analyzing the health situation and evaluating health services<sup>28,29</sup>.

The State of Acre may still suffer from underreporting of births and deaths, underestimating the numbers of live births and deaths (due to births and deaths at home or in remote areas). However, in the city of Rio Branco, the state capital, thanks to a well-structured healthcare network and the small number of home births and deaths, it is unlikely that the phenomenon of underreporting compromised the study's results. The quality of data on pregnancy in the SINAN could also be questioned, but the searches by telephone contact tended to minimize this potential weakness.



Furthermore, the study's temporality allowed identifying inconsistencies and cases of incomplete data in the respective databases. Despite advances in processing computerized data, there is still a need for improvements in completing the data collection instruments that feed health information systems. Such improvements should feature investment in training and capacity-building of technical teams and their infrastructures.

## Conclusion

According to the study's results, dengue virus infection during pregnancy can be considered a risk factor for both the mother and infant. Pregnant women in the city of Rio Branco who were exposed to the dengue virus showed an increased risk of complications, including maternal, neonatal, and infant deaths, when compared to pregnant women not exposed to the virus. Fetal deaths were also observed in the group of exposed pregnant women, strongly suggesting the need for close monitoring of pregnant women with dengue virus infection.

## Contributors

H. A. C. Feitoza were responsible for the elaboration of the research project, data collection, data analysis and writing of the scientific paper. S. Koifman and R. J. Koifman contributed in all stages of the work and participated in the write and review of the project and paper. V. Saraceni participated in the revision of the final version of the scientific paper.

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## Resumo

Os efeitos da infecção por dengue na gestação são desconhecidos em Rio Branco, Acre, Brasil. O objetivo deste trabalho é determinar os riscos de complicações maternas, fetais e infantis decorrentes da infecção por dengue durante a gestação. Estudo de coorte de gestantes expostas e não expostas ao vírus do dengue no período 2007-2012. Foram estimadas incidências e razões de risco de complicações maternas, fetais e infantis. Na coorte exposta houve 3 óbitos fetais e 5 neonatais. Dois óbitos maternos foram identificados na coorte exposta, desfecho ausente no grupo não exposto ( $p = 0,040$ ). A coorte exposta apresentou uma razão de riscos –  $RR = 3,4$  (IC95%: 1,02-11,23) para óbito neonatal. Em relação ao desfecho óbito neonatal precoce, a razão de riscos observada foi de 6,8 (IC95%: 1,61-28,75). Dez óbitos infantis ocorreram nos filhos de gestantes expostas e 7 nos de não expostas ( $RR = 6,0$ ; IC95%: 2,24-15,87). As mulheres infectadas com o vírus do dengue na gestação apresentaram uma razão de riscos maior em relação à ocorrência de óbitos maternos, neonatais e infantis.

Dengue; Gravidez; Mortalidade Materna;  
Mortalidade Infantil

## Resumen

Los efectos de la infección por dengue en la gestación son desconocidos en Río Branco, Acre, Brasil. El objetivo de este trabajo es determinar los riesgos de complicaciones maternas, fetales e infantiles, derivadas de la infección por dengue durante la gestación. Estudio de cohorte de gestantes expuestas y no expuestas al virus del dengue durante el período 2007-2012. Se estimaron incidencias y razones de riesgo de complicaciones maternas, fetales e infantiles. En la cohorte expuesta hubo 3 óbitos fetales y 5 neonatales. Dos óbitos maternos fueron identificados en la cohorte expuesta, desenlace ausente en el grupo no expuesto ( $p = 0,040$ ). La cohorte expuesta presentó una razón de riesgos  $RR = 3,4$  (IC95%: 1,02-11,23) para el óbito neonatal. En relación con el desenlace óbito neonatal precoz, la  $RR$  observada fue de 6,8 (IC95%: 1,61-28,75). Diez óbitos infantiles se produjeron en los hijos de gestantes expuestas y 7 en los de no expuestas ( $RR = 6,0$ ; IC95%: 2,24-15,87). Las mujeres infectadas con el virus del dengue en la gestación presentaron una razón de riesgos mayor, en relación a la ocurrencia de óbitos maternos, neonatales e infantiles.

Dengue; Embarazo; Mortalidad Materna;  
Mortalidad Infantil

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