

Obese pregnant women infected by Zika virus have impaired immune response, shows study

April 19 2023, by Maria Fernanda Ziegler



Anna Cláudia Castello Branco (ICB-USP), first author of the article in *Viruses*, with the results. Credit: Maria Notomi Sato

Researchers at the University of São Paulo (USP) in Brazil have shown for the first time that gestational obesity associated with infection by Zika virus influences the placenta's antiviral response, weakening the organ's capacity to attack the pathogen and protect the fetus.

The study results are reported in an article published in the journal *Viruses*.

According to the authors, the findings underscore the importance of adequate antenatal care. "We normally associate [obesity](#) during [pregnancy](#) with problems such as gestational diabetes or high birth weight infants, but it should be stressed that the consequences can go beyond these. We proved in this study that the placenta's immune response, or rather the immune response that occurs at the maternal-fetal interface, is highly compromised in these cases," said Maria Notomi Sato, a professor at USP's medical school and last author of the article.

In cases of Zika infection in obese pregnant women, she explained, transcription of genes and production of proteins involved in the immune response are both diminished. "Above all, the interferon pathway is impaired. The protein interferon helps inhibit replication of the virus and is an extremely important part of the response to any viral disease," she said.

It should be noted that Zika, like dengue and SARS-CoV-2, is able to cross the placental barrier and infect the baby. The group analyzed 30 placenta samples from obese and non-obese pregnant women infected by Zika supplied by Oswaldo Cruz Foundation (FIOCRUZ), a research institution subordinated to the Brazilian Ministry of Health, and 39 from healthy women, supplied by Patrícia Rondó, a researcher at USP's School of Public Health who is conducting a population study of pregnant women in Araraquara, São Paulo state.

The analysis showed that Zika can alter the placenta morphologically in obese pregnant women and aggravate insufficiency of the placental type I interferon pathway. As an immune evasion strategy, the virus inhibits activation of intracellular receptors that detect viral RNA and trigger type I interferon production, such as RIG-I, IRF-3 and MAVS.

Interferons are a broad class of cytokines elicited to defend the organism and are essential for mobilizing the immune response to pathogens, activating genes that impair their replication.

Another evasion mechanism used by Zika is degradation of the protein STAT2, which mediates interferon signaling. The study showed that these evasion strategies enabled the virus to persist in placenta, facilitating its replication and transmission to the fetus.

"Analysis of the placenta samples showed that in non-infected obese pregnant women there were no alterations in transcriptional expression of antiviral factors or expression of types I and III interferon. In obese pregnant women who contracted Zika, we observed a decrease in transcriptional expression of RIG-I and IFIH1 [the precursor gene for the protein MDA-5]. This decrease resulted in a weakened antiviral response," said Anna Claudia Castelo Branco, first author of the article and a Ph.D. candidate in the Department of Immunology at USP's Biomedical Sciences Institute.

Microcephaly

The study did not find a link between gestational obesity and infant microcephaly. "It wasn't possible to show such a link because the study involved a small number of samples," Castelo Branco said. "Previous research had found Zika infection in the first or second trimester to be most critical for the occurrence of microcephaly owing to issues relating to the neural development of the fetus. We had a larger number of

samples from obese pregnant women who were infected in the third trimester."

Risk factors such as the timing of the infection during pregnancy and whether it was a primary infection, reinfection or chronic infection, as well as membrane rupture and birth type, can influence the incidence of fetal transmission, she added.

Obesity is a state of chronic inflammation that causes multiple metabolic diseases, she went on: "It's as if all the components of obesity—adipocyte hyperplasia, fat accumulation, altered gut microbiota—make the organism constantly inflamed. However, the inflammation is low-grade, so the immune system is always on alert in a succession of false alarms."

Obesity in general (not in the context of pregnancy) has been found to correlate with impaired responses to infections and vaccines, and it is a risk factor for many diseases.

"In the context of pregnancy, few studies have so far found a link between obesity and a higher risk of infections. Our study is the first to prove that the placenta's [immune response](#) is weakened in obese women infected by Zika," Castelo Branco said.

More information: Anna Cláudia Calvielli Castelo Branco et al, Obesity Induces an Impaired Placental Antiviral Immune Response in Pregnant Women Infected with Zika Virus, *Viruses* (2023). [DOI: 10.3390/v15020320](#)

Provided by FAPESP

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