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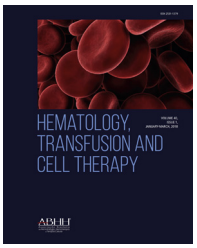

Original article

Risk of Zika virus transmission by blood donations in Brazil

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ABSTRACT

Background: Zika, a disease caused by Zika virus infections, has recently emerged and caused outbreaks in many parts of the world. The clinical manifestations of Zika are usually mild, mostly presenting as an exanthematic febrile disease, but on some occasions, it might be associated with microcephaly after intrauterine infection, and Guillain-Barré Syndrome. Zika virus is primarily transmitted by mosquito bites, but other means of transmission have been described, and potential risk for blood transmission has been reported in French Polynesia and Brazil.

Methods: To investigate the risk of Zika virus infection after a blood transfusion in an area of Brazil where a possible transmission by a platelet concentrate has been described. Using a mini-pool format, 1857 blood donations were evaluated by real-time reverse transcriptase polymerase chain reaction designed to detect Zika virus RNA.

Results: After testing samples individually from positive mini-pools, the prevalence of Zika virus RNA was only 0.16%, a result probably associated to the low circulation of this virus in the study area. In addition, it was evident that the implementation of post-surveillance programs is important to detect Zika virus infections in blood donors, as the post-donation surveillance program detected two blood donors with the disease in this study.

Conclusion: This study shows that the risk for Zika virus transmission by blood transfusion is real, even in regions with a low circulation of the disease, but the combination of the detection of Zika virus RNA by polymerase chain reaction and post-donation surveillance might reduce the risk of transmission by blood transfusions.

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Introduction

Zika, a disease caused by the Zika virus (ZIKV), is usually characterized by rash, low-grade fever and mild constitutional symptoms.[1,2] However, according to data released from studies in French Polynesia, most ZIKV infections remain asymptomatic.[3] Although the prevalence of asymptomatic ZIKV infections in Brazil is not known, infections by this virus were first reported as a dengue-like disease in 2015 and since then, significant outbreaks have occurred in several regions of the country, especially in the northeastern region.[4] Although hard data are still missing, there is evidence that ZIKV infections might also be associated with more severe presentations, such as Guillain-Barré Syndrome and microcephaly in newborn babies whose mothers were infected with ZIKV during pregnancy. This arthropod-borne virus is primarily transmitted by the bites of female *Aedes* mosquitoes, but new transmission routes have been described in outbreaks occurring in the Pacific region and the Americas.[5–7] Interestingly, the first isolated and fully sequenced autochthonous transmitted ZIKV in the Americas came from a region where the Zika outbreak has not been very significant, the southeastern region of Brazil.[8] This virus was isolated in the city of Campinas, São Paulo State, in a patient who underwent a liver transplantation and received a platelet concentrate transfusion with probable transfusion transmission being reported.[9] Due to this local transmission and the report from French Polynesia on the risk of ZIKV transmission by blood,[5] it is of paramount importance to define the real risk of ZIKV transmission either through blood or blood components, and which preventive measures should be taken to minimize this risk. This study reports the results of an investigation to detect the frequency of ZIKV RNA using minipools comprised of blood donated in the same city where the first Brazilian ZIKV was isolated, and reinforce the importance of post-donation surveillance to detect ZIKV infections in blood donors.

Objectives

To identify the prevalence of ZIKV RNA in blood donations in the blood center of the Universidade Estadual de Campinas (UNICAMP).

Methods

Blood donors

A total of 1857 blood donations from the Campinas metropolitan region were screened for ZIKV RNA by real-time reverse transcription polymerase chain reaction (rRT-PCR). Samples were collected from all donations on Fridays for four consecutive weeks in February and March 2016. According to the Municipal Epidemiological Surveillance Agency[10] the highest incidence of arthropod-borne diseases is in the summer and thus, it is believed that this would be the best time to investigate ZIKV transmission by blood transfusion. During the pre-donation evaluation, donors were asked about symptoms of infectious diseases in the weeks leading up to the interview, known risk factors for viral infections and having been in areas of risk for Zika outside of Brazil in the previous 30 days. The blood donations were screened for the usual bloodborne pathogens. The blood components produced from these donations would be released for transfusion independently of any screening test for ZIKV RNA. This study was approved by the Ethics Committee on Human Research of the Faculdade de Medicina de Ribeirão Preto of the Universidade de São Paulo (FMRP USP). The complementary tests were authorized by the donors who signed informed consent forms before the blood donation.

RNA extraction and real-time reverse transcription polymerase chain reaction

The nucleic acids were extracted on the same day as the donation from minipools containing samples from six blood donors using a silica membrane protocol developed by BioManguinhos (Rio de Janeiro, Brazil) and an automated, robotic system [BioRobot MDx Universal System (Qiagen, Switzerland)]. ZIKV RNA detection as well as NAT screening for human immunodeficiency virus-1 (HIV-1), Hepatitis C virus (HCV), and hepatitis B virus (HBV) were performed in minipools of donations using the NAT HIV/HCV/HBV Kit (Bio-Manguinhos, Rio de Janeiro, Brazil). Extracted RNAs were frozen at −80 °C and ZIKV RNA testing was performed after 24–36 h. In order to obtain the most reliable rRT-PCR results, Lanciotti's rRT-PCR protocol was initially used and confirmed by the rRT-PCR protocol described by Pyke et al.[2,11] Samples were considered positive if they amplified ZIKV RNA with a crossing threshold (CT) of less than 40 and samples with a CT between 35 and 40 were submitted to confirmation tests by an additional rRT-PCR. Donor samples in rRT-PCR positive pools were tested individually to identify the positive donor. All rRT-PCR included internal control samples that tested positive for the HIV-1, HCV and HBV genomes, and positive ZIKV controls consisting of dilutions of ZIKV prepared in Vero cells. In short, rRT-PCR for ZIKV used 4 μL aliquot from each minipool and 6 μL of amplification reaction containing 2.5 μL of reaction mix (TaqMan Fast Virus 1-Step Master Mix), and 125 nM of each primer and probe diluted in nuclease free water.

Sequencing and phylogenetic analysis of the Zika virus detected in positive samples

Positive samples were sequenced by Sanger technology, using the BigDye Direct Cycle Sequencing kit protocol and primers that amplify a 500-base pair region inside the *NS1* gene of the ZIKV. Sequencing was performed in an ABI 3500 sequencer (Applied Biosystems) and data was analyzed using MEGA 7 software. The analysis involved 13 *NS1* gene sequences from distinct ZIKV sequences available in the NCBI website. A total of 474 positions were analyzed in the final dataset because all positions containing gaps and missing data were eliminated.

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