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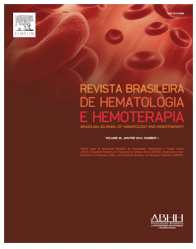

Letter to the Editor

Zika virus and its implication in the transfusion safety

Zika virus (ZIKV), an emerging flavivirus, was initially isolated in 1947 from a Rhesus monkey in Uganda. The first evidence of human transmission of ZIKV was reported in 1952.[1] Only sporadic cases of ZIKV in humans were reported in Africa and Asia before 2007, when significant outbreaks were registered outside these regions – on the islands of Micronesia, French Polynesia and New Caledonia in the Pacific Ocean.[2] In Brazil, the first autochthonous ZIKV transmission was reported in the northeastern region in May 2015.[3] It is believed that ZIKV was introduced in Brazil by asymptomatic travelers during the 2014 World Cup or by the World Sprint Championship canoe race.[4,5] ZIKV has similar characteristics to Dengue virus in relation to epidemiology and the transmission cycle in urban environments.[6] Therefore, we should expect that, due to the large distribution of the arthropod vectors (*Aedes aegypti* mosquitoes), the number of outbreaks and symptomatic cases might propagate.

In Brazil, there are 17 officially confirmed ZIKV cases in three states: Bahia, Rio Grande do Norte and São Paulo.[7] However, with the spread of ZIKV in the country, the World Health Organization (WHO) has already reported ZIKV disease in 14 Brazilian states including Alagoas, Bahia, Ceará, Maranhão, Mato Grosso, Pará, Paraíba, Paraná, Pernambuco, Piauí, Rio de Janeiro, Rio Grande do Norte, Roraima, and São Paulo.[8] Currently, Brazil is evidencing a high number of cases of microcephaly, mainly in the northeastern part of the country, which was believed to be linked to ZIKV infection acquired during pregnancy. However, this cannot be confirmed due to insufficient scientific support as ZIKV RNA was found in the amniotic fluid of only two cases (unofficial source). If this condition is found to be related to ZIKV, it will represent a novel clinical manifestation of this emerging virus. Other neurological disorders correlated to ZIKV manifestations include: Guillain-Barré syndrome, encephalitis, myelitis, meningoencephalitis, and optical neuritis.[9]

Since ZIKV is an blood-borne virus transmitted by arthropods, it represents potential risk for transfusion safety. Although the significance of ZIKV to the blood transfusion process and use of blood derivatives is currently unknown, there is a risk that ZIKV could also be transmitted by transfusions. A high number of asymptomatic blood donors was observed during the French Polynesia outbreak. However, several questions remain unclear related to the possible impact of ZIKV in blood transfusion and transfusion medicine in general:

1. *The potential of ZIKV to cause asymptomatic cases must be elucidated*. Asymptomatic cases of ZIKV among blood donors (up to 74%) have been reported.[10] Therefore, the potential of transmission by transfusion exits. To calculate the transfusion-transmission model, it is important to estimate the incidence of infection and the average duration of viremia.[11] However, even at a global level, there is no information about the incidence of infection in the general population and the events related to the viremic phase of ZIKV infection.
2. *Viral load of ZIKV infection*. Viral load during ZIKV infection has previously been measured in blood samples of asymptomatic blood donors (3.40–6.91 log copies/mL).[12] Additionally, viral load has been detected in urine 10 to 20 days after the onset of the disease ($0.7–220 \times 10^6$ copies/mL).[13] Therefore, transfusion-transmitted ZIKV infection is possible. However, more detailed studies concerning to the quantity and viremia period in asymptomatic individuals are essential.
3. *Effectiveness of transmission via blood transfusion*. Until now, the effectiveness of the transmission of ZIKV via transfusion of blood is unknown. As other flaviviruses, such as Dengue virus 1–4 and West Nile virus,[11] can be transmitted by blood transfusion and cause clinical symptoms in blood recipients,[14] the transmission of ZIKV by transfusions seems possible.
4. *Inactivation of ZIKV in blood*. It seems that ZIKV is sensitive to blood pathogen inactivation procedures. The application of amotosalen and ultraviolet A illumination reduces viral titers in plasma and ZIKV does not productively infect cell cultures. In addition, by the second passage in cell cultures, ZIKV RNA becomes undetectable.[15] Therefore, the procedures of pathogen inactivation in blood seem to be effective to inactivate ZIKV and prevent transfusion-transmitted infection.

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5. *Molecular diagnosis of ZIKV during screening for blood donation.* In Brazil, no serological or molecular tests for ZIKV have been approved by the Ministry of Health. The diagnosis is currently made by isolation of the virus in cell cultures and molecular detection by in-house polymerase chain reaction systems in Reference Laboratories. The immediate implantation of molecular tests to screen blood donors at this moment seems unfeasible. This is not only due to the high cost of molecular testing but also by the fact that the pathogenesis of ZIKV infection is not fully understood. Moreover, ZIKV infection is seasonal as more cases are reported during the peak proliferation period of the transmitting arthropod vectors, therefore the implementation of blood donor screening for ZIKV should follow the seasonality of infection.
6. *Conduct and deferral of blood donors from donation.* Brazilian blood banks should intensify the pre-donation screening to minimize the risk of the transmission of ZIKV by transfusions. It is important to pay attention to possible disease risk factors (signs and symptoms of an arboviral disease, travel to endemic areas, etc.) in blood donor candidates. We also recommend that blood banks offer educational programs about ZIKV infection to alert about the potential risk of the transmission of this emerging virus.

Conclusion

ZIKV is an emerging virus in Brazil. In the majority of cases, the infection is asymptomatic however mild to severe clinical symptoms have also been described. The efficiency of the transmission of ZIKV by transfusions is still unknown and additional studies are needed to better evaluate the proportion of asymptomatic blood donors infected by ZIKV, the duration of viremia before clinical signs of acute arboviral infection appear, and the clinical outcomes of ZIKV infection. Until now, the only preventive measures to control ZIKV infection are stringent vector control and individual precautions in respect to mosquito bites.

Conflicts of interest

The authors declare no conflicts of interest.

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