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Postdonation information during dengue outbreaks at a single blood center in Brazil: An ally against transfusion-transmitted infections

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Abstract:

BACKGROUND: Brazilian blood banks encourage donors to report postdonation information (PDI) regarding conditions that would lead to deferral in an attempt to retrieve distributed nonconforming blood.

OBJECTIVES: This study evaluated the profile of donors reporting PDI, the impact on transfusion safety, and the possible impact on the discard of blood products.

SUBJECTS AND METHODS: We analyzed 115 consecutive PDIs between May 2014 and July 2015, a period comprising two dengue-like syndrome (DLS) outbreaks.

RESULTS: These PDIs accounted for 87,780 blood donations. The average time for PDIs since donation was 4 (0–23) days and 190 blood components were discarded. DLS accounted for 21.7% of the PDIs analyzed; 11 of the 23 samples tested were nucleic acid test (NAT) positive for dengue and 2 positive for *Zika virus* (ZIKV). Six of these PDIs were reported after blood components have been transfused: After NAT testing, one of these recipients was diagnosed with dengue and another one with ZIKV infection, both possible transfusions transmitted but without clinical consequences.

CONCLUSION: The high number of recovered blood components due to PDI suggests that PDI remains a great ally in the fight against transfusion-transmitted infections and may be particularly useful during outbreaks of emerging potentially blood-borne pathogens.

Keywords:

Dengue, postdonation information, transfusion-transmitted infection, *Zika virus*

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Introduction

Postdonation information (PDI) is a valuable tool for hemovigilance and may considerably increase transfusion safety. PDI can be defined as any information given by blood donors to the blood center after the donation and that could potentially pose risks to the quality of the blood components or to recipients' safety.[1] The source of PDI may be as follows: (1) information given by the donors themselves, (2) information from laboratory testing centers that identify transfusion transmissible infections in subsequent donations, and (3) information from other blood banks or medical services.[2]

Through this mechanism, donor conditions that should lead to deferral but may occur after the time of donation are reported, enabling the implementation of safety measures such as proper evaluation of the recipients or the recovery of blood products not yet transfused.[3]

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In Brazil, blood donors are instructed to report to blood centers any symptoms or signs suggestive of infection that may arise in the days following donation. This measure seems particularly important considering the recent and recurrent arboviruses outbreaks such as dengue, Zika, and chikungunya, occurring in this region.[4] Notably, the emergence of *Zika virus* (ZIKV) aroused extreme concern about the safety of patients receiving blood transfusions since the potential for transmission and infectivity of the virus by transfusion have not yet been fully elucidated. Nevertheless, there are reports of possible transmission of ZIKV through blood transfusion, which were unraveled through investigations conducted after the PDI.[5,6] Transfusion transmission of the dengue virus (DENV) has already been documented, including clinical repercussions on the recipients.[7-9] In the case of the chikungunya virus, there is, at present, no epidemiological evidence of its transfusion transmission.

Thus, the aim of this study was to evaluate the profile of donors reporting PDI in a Brazilian blood bank, including the results of testing by nucleic acid test (NAT) technology and outcomes presented by the recipients of these transfusions, as well as the possible impact of the discard of blood products. We were able to demonstrate that the registration of PDI allowed proper recovery and discard of blood products potentially containing arbovirus, ensuring greater safety for blood transfusion recipients at our institution.

Subjects and Methods

Study population

This is a single-center study that retrospectively evaluated stored blood samples from donors who reported PDI at the Hematology and Transfusion Medicine Center of Campinas, Brazil, between May 1, 2014 and July 31, 2015. All consecutive PDIs recorded at the institution were submitted to evaluation by transfusion medicine specialists according to specific institutional protocols that include quarantine, lookback, market withdrawal, and recalls. According to Brazilian government regulations, all donors were instructed to contact the blood center if symptoms or signs of infection like fever or diarrhea occur within at least 7 days after donation. All donors underwent a predonation questionnaire and blood was collected only from voluntary donors who were asymptomatic at the time of donation. A signed informed consent statement was obtained from all the participants (the informed consent term for blood donation contemplates the possibility of performing tests for emerging pathogens, even if not mandatory by law).

PDI was reported at any time after blood donation, by a donor or a third party, and from any cause that justifies or not an action, regardless of the time elapsed since the donation. There were no exclusion criteria for the registration of PDI.

The study period comprised two dengue outbreaks in the state of São Paulo, whose highest incidence was reported from March to May 2014 and 2015, according to the local epidemiological records.[4]

Postdonation information categorizing

PDI reports were divided into three groups: PDI by nonspecific infection, dengue-like syndrome (DLS), and other causes. The first group comprised those PDIs whose complaints contemplate signs and symptoms related to bacterial infections such as diarrhea, pharyngitis, tonsillitis, or other infectious processes necessarily accompanied by fever. The second group comprised signs and symptoms that raised clinical suspicion of dengue based on clinic-epidemiological and/or laboratory criteria. The last group comprised PDI that did not fit in the above infectious PDI groups.

Collection of clinical and laboratory data

Clinical and laboratory data were obtained from the forms filled in at the time of PDI. The final status of blood products was retrieved from the computerized system. If necessary, donor and the blood component recipient were reevaluated directly or indirectly by the transfusion medicine specialist team for clinical evaluation and data collection. Particularly with regard to the PDI data used in the central analysis of this work, it is important to note that in our blood bank, internal and external audits are held annually for all of the operational procedures, including the PDI process.

In addition, all samples from donations related to DLS PDI were tested for the presence of dengue, chikungunya, and ZIKV, using the remaining sera tested for blood-borne diseases during blood donation or stored fresh frozen plasma (FFP) units.

Molecular assessment for dengue, Zika, and chikungunya

A multiplex real-time polymerase chain reaction (PCR) (NAT) was performed using an assay developed by Bio-Manguinhos/Fiocruz for the detection of Zika (ZIKV), chikungunya (CHIKV), and dengue (DENV) on clinical samples tested on a single Kit (Molecular ZDC, Bio-Manguinhos/Fiocruz, Brazil).

RNA was isolated from serum samples using MDx equipment (Qiagen, Germany) according to the manufacturer's instruction. The multiplex one-step real-time PCR setup was performed automatically with Janus instrument (PerkinElmer, USA), and the

amplification was carried on the sequence detection system ABI 7500 (Life Technologies, USA). Positive control for ZIKV, CHIKV, and DENV was used in every assay. An internal control (IC, patent PI0600715-5, Bio-Manguinhos/Fiocruz, Brazil) was used to control all steps and reactions.

The amplification conditions were 30 min at 51°C, 10 min at 95°C, and 40 cycles of 30 s at 95°C and 1 min 60°C. Samples were considered negative if the IC was positive, but the signal for ZIKV, CHIKV, and DENV was negative.

Statistical analysis

Descriptive statistics summarize the characteristics of donors and PDI profile. Results are presented in the form of central tendency and variance.

Results

Characteristics of donors and postdonation information

One hundred and fifteen PDIs were recorded between May 1, 2014 and July 31, 2015. Demographic and clinical characteristics of these donors and their PDI are shown in Table 1.

The 115 PDIs accounted for 87,780 blood donations, related to 249 blood components produced: 17 whole blood (WB) units, 95 red blood cell (RBC) concentrates, 44 platelet concentrates (PCs), and 93 FFP units. Blood donors who reported PDI were an average 33 years old (18–56) and there was a female predominance (61.7%). PDI was more frequently reported by repeat donors than first-time or sporadic donors. During the study period, PDI was reported at a prevalence of 1:763 blood donations, with increasing incidence in the months of dengue outbreaks (e.g., March and April/2015, more than 20 PDI/month) [Figure 1a].

Regarding the causes of PDI, there was a predominance of nonspecific infections (50.4%). The DLS group was responsible for 25 cases (21.7%). The remainder PDI reports (27.8%) were allocated in the group "other causes" such as viral syndromes not associated with fever, recent vaccination, postdonation fatigue, postdonation hematoma, travel to endemic areas for malaria or West Nile Virus, or request for discarding due to information on exposure to sexual risk omitted by blood donor at the time of interview [Figure 1b].

Of note, samples of all recovered products related to infectious PDI were sent to quality control with negative bacterial testing (BacT/ALERT® PF, bioMerieux, USA, or eBDS system, Haemonetics, USA).

Table 1: Postdonation information details, blood donor characteristics and blood components discarded from May 2014 to July 2015 (*n*=115)

Characteristics	*N*
Donor age (year), median (range)	33 (18-56)
Donor gender, male/female, *n* (%)	44/71 (38.3/61.7)
Type of donor, *n* (%)	
Repeated donors	71 (61.7)
First-time or sporadic donors	44 (38.3)
Frequency of PDI, *n*	
PDI:donations	1:763
Maximum PDI/month (month, year)	20 (March, 2015)
Minimum PDI/month (month, year)	4 (December, 2014)
Related blood components to PDI, *n*	
WBU	17
RBC	95
PC	44
Apheresis platelets	1
FFP	93
PDI causes, *n* (%)	
Nonspecific infection	58 (50.4)
DLS (cases confirmed by clinical-epidemiological criteria and/or laboratory)	25 (21.7)
Others causes	32 (27.8)
Fever reported in PDI, *n* (%)	61 (53)
PDI days since donation, median (range)	
Nonspecific infection + other causes	4.6 (0-23)
DLS	6.3 (1-23)
Discarded blood components due to PDI, *n*	
WBU	15
RBC	73
PC	25
FFP	77

PDI=Postdonation information, WBU=Whole blood units, RBC=Red blood cells concentrates, PC=Platelet concentrate, FFP=Fresh frozen plasma, DLS=Dengue-like syndrome

Postdonation information impact on discard of blood products

One hundred ninety blood components were discarded due to PDI during the study period. Of these, 15 units were WB, 73 RBC, 77 FFP, and 25 PC. There was an evident increase in discard during the dengue outbreak period (March/April 2015) as seen on Figure 1b.

Viremia in asymptomatic donors as a possible risk of disease transmission

The evaluation of DLSs for dengue, chikungunya, and ZIKV (21.7% of PDI) revealed that of the 23 samples tested by NAT, 11 were reactive for DENV and 2 for ZIKV. Ten samples were negative when tested for arboviruses.

The average time of PDI registration since the onset of dengue-like symptoms was 4 days (range: 1–5) in the nonreactive group and 2 days in the positive group (range: 0–4). Four donors have failed to specify the precise time elapsed since the donation until the onset

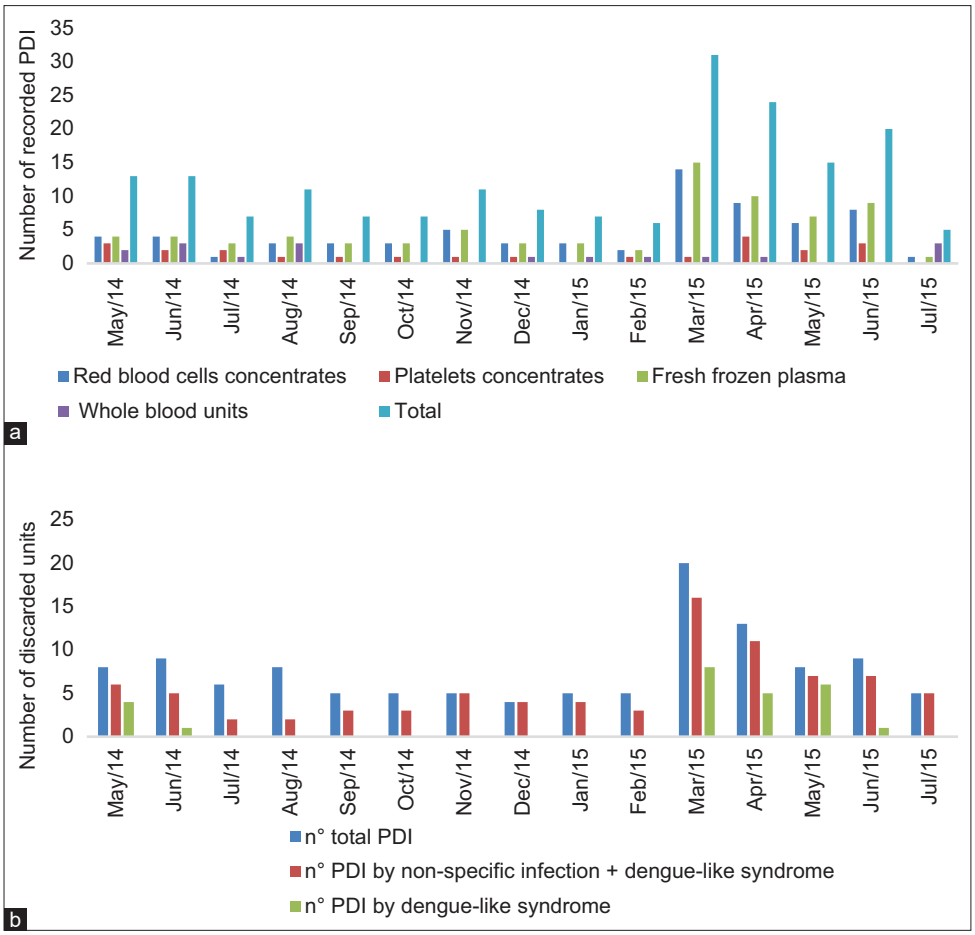

Figure 1: Monthly distribution of the postdonation information causes, separated by blood product type (a) and discarded blood components due to postdonation information during the study period, separated by type of postdonation information record (b)

of dengue-like symptoms. Due to logistical problems such as lack of available aliquot or stored FFP unit, two samples were not tested molecularly.

Considering DLS PDI, nine blood products (3 RBC and 6 PC) were transfused before the donors registered PDI. Of the transfused blood components, the majority (four cases, 44.4%) resulted in the absence of clinical consequences in the recipient, three cases (33%) have not been evaluated by the absence of feedback from the receptor, and 2 (22%) of transfused blood components were responsible for perceived mild symptoms (thrombocytopenia and fever) in the absence of other causes that justify these symptoms. We concluded retrospectively, through serological and NAT evaluation of the donor and recipient, that one of the cases of possible dengue in fact corresponded to ZIKV.[5] PDI cases with the potential risk of arbovirus transfusion transmission are detailed in Table 2.

Discussion

Since its establishment in France in 1993, the practice of hemovigilance has become a key element to achieve adequate blood transfusion safety by analysis of incidents and adverse events related to transfusion.[10] An important part of hemovigilance is the lookback investigation of events related to PDI reported by blood donors who have any signs or symptoms after donation that were absent at the time of the predonation screening.[11]

PDI becomes particularly important when considering the possibility of outbreaks of emergent pathogens. This could be evidenced, for example, during Q fever and Creutzfeldt–Jakob disease outbreaks in Europe, enabling the disposal of potentially infected blood products and communication to the industries of plasma-derived products.[12,13]

In recent years, Brazil has seen various outbreaks of arboviruses with potential for transfusion transmission, such as dengue and chikungunya, and more recently, ZIKV. In the specific case of ZIKV, its infecting potential is not fully elucidated, but great concern arised in blood banks worldwide since donors may present asymptomatic infections, preventing recognition of many infected individuals by clinical screening only.

In this context, the role of (PDI) becomes even more relevant. In our center, we had 115 PDIs reported during the

Table 2: Details of blood products receptors cases involved in post donation information "dengue-like syndrome" and the possible transfusion-transmitted infections

Days after donation to PDI registration (month/year)	Onset of dengue-like symptoms	Blood components transfused	PCR-CT	Clinical impact
May 23, 2014	#	PC	26.38 (DENV)	Not evaluated
March 3, 2015	At the day of donation	PC	21.9 (ZIKV)	ZIKV transmission (thrombocytopenia and fever)
March 1, 2015	At the day of donation	PC	32.12 (DENV)	DENV transmission (thrombocytopenia and fever)
March 7, 2015	2 days after donation	RBC	32.12 (DENV)	No impact
March 4, 2015	2 days after donation	PC	28.85 (DENV)	Not evaluated
April 12, 2015	4 days after donation	RBC	Undetectable	No impact
April 4, 2015	4 days after donation	PC	33.47 (DENV)	No impact
May 13, 2015	4 days after donation	RBC	Undetectable	Not evaluated
June 5, 2015	3 days after donation	PC	Undetectable	No impact

#Donors have failed to specify the precise time elapsed since the donation until the onset undetectable of dengue-like symptoms. RBC=Red blood cell, PC=Platelet concentrate, PDI=Post donation information, CT=Cycle threshold, PCR=Polymerase chain reaction, DENV=Dengue, ZIKV=Zika virus

study period (May 1, 2014 and July 31, 2015), leading to the disposal of 190 blood components. Of the 115 notifications, 21.7% corresponded to donors who reported symptoms suggestive of dengue. In such cases, of the 23 samples tested by PCR, 11 resulted positive for dengue (DENV) and 2 were positive for (ZIKV). Six PDI notifications related to DLS were reported after the blood components have already been transfused. The investigation of these recipients led to the diagnosis of dengue infection in one of them, and another one was diagnosed with ZIKV infection, the two cases considered to be related to transfusion.

Conclusion

Therefore, our results emphasize the importance of stimulating PDI notification by blood donors. In the specific case of our center, this tool enabled the discard of a large number of potentially contaminated blood components before they were transfused. This measure certainly reduced the possibility of serious adverse events in potentially vulnerable recipients. Moreover, this instrument makes it possible to generate warning about those patients who were transfused by blood products prior to the acquisition of this information, allowing medical staff to anticipate surveillance measures and treatment, if needed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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