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Seroprevalence and factors associated with IgG anti-DENV positivity in blood donors in Burkina Faso during the 2016 dengue outbreak and implications for blood supply

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Summary

Objectives: Our study aimed to update the seroprevalence and factors associated with anti-dengue virus (DENV) antibody positivity among blood donors and to discuss their implications for blood supply.

Background: Questions on the potential transmission of DENV by transfusion increased after the documentation of the risk of transmission of the West Nile virus. This risk was estimated after transfusion of DENV RNA-positive blood units of up to 37.5%. In Burkina Faso, very few studies on DENV in blood donors have been conducted. As a result, there were no reliable data on DENV to allow the implementation of appropriate measures to control the risk of transmission of the dengue virus by blood transfusion.

Methods: We conducted a 4-week cross-sectional study from December 4 to 30, 2016. Blood donors of both genders, aged 18-60 years, accepted for blood donation after medical selection were consecutively enrolled.

Results: Our study included a total of 1007 blood donors, in which donors living in urban areas represented 78.2%. The mean age was 26.1 ± 8.1 years. After adjustment in a multiple regression logistic model, the odds of having IgG anti-DENV increased as age increased. The odds of DENV was 53% lower in rural areas (OR = 0.47; P = .000) compared to urban settings and 42% lower in mobile sites (OR = 0.58; P = .03) compared to fixed ones.

Conclusion: Our study provides new and useful insights for future research on the risk of TT-DENV throughout blood transfusion.

KEYWORDS

anti-DENV antibodies, blood donation, dengue, transfusion-transmitted infections

Globally, dengue infections constitute a significant public health burden. Nearly two-thirds of the global population is at risk,[1] mainly in African, Asian and American inter-tropical developing countries. In the last half century, the prevalence of the dengue virus (DENV) has increased dramatically (up to 30%) worldwide,[2,3] especially in Sub-Saharan Africa.[4-6] In Sub-Saharan Africa, dengue fever represents an added

underestimated burden to an infectious disease landscape dominated by malaria.[2,7,8] In this context, febrile illnesses, including dengue, are likely to be misdiagnosed and treated as malaria. This negatively impacts the knowledge of dengue fever epidemiology.[9]

The first dengue epidemic known in Burkina Faso occurred in 1925.[4] Since then, a significant number of cases was reported in the 1980s,[10] in the 2000s[11] and, more recently, during the 2013 and 2015 outbreaks.[7,8,12,13] In 2016, Burkina Faso experienced another dengue outbreak. The majority of cases (82.3%) were recorded in Ouagadougou.[14] This recent rapid expansion throughout the world and in Burkina Faso is associated with factors such as rampant population growth, unplanned urbanisation and the circulation of people and goods.[7]

The asymptomatic and subclinical cases, estimated at around 50-85% of DENV infections, constitute the main concern regarding transfusion safety as symptomatic cases are assumed to be rejected at the pre-donation screening[15] Previous studies reported the presence of DENV in blood donors in Honduras, Brazil, Australia,[16] Puerto Rico[17,18] and Saudi Arabia.[19,20] Viraemic donor rate may be as high as 0.4% during outbreaks,[21] with a risk of transfusion-transmitted DENV (TT-DENV) calculated as 1 in 1300 donations in Puerto Rico.[22]

Questions on the potential transmission of DENV by transfusion increased after the documentation of the risk of transmission of the West Nile virus (WNV) by Biggerstaff & Petersen[23] and Biggerstaff & Petersen.[24] It seems highly probable that DENV is transmitted in a manner similar to the WNV as both are arboviruses within the same family of *Flaviviridae*.[25] Many cases of DENV TT were documented in Hong Kong,[26] in Singapore,[27] in Puerto Rico[18] and in Brazil.[28,29] Sabino et al. estimated that the DENV TT rate after transfusion of DENV RNA-positive blood units was 37.5%.[21]

Despite the endemo-epidemic character of DENV in Africa,[4-6] there are scarce data on DENV concerning blood transfusion. Surveys carried out in Zanzibar by Vairo et al.[30] and in Ghana by Narkwa et al.[31] showed seroprevalences among blood donors of 50.6% and 43.6%, respectively. In both studies, the authors reported high seroprevalence of DENV infection in donors living in urban areas. However, their findings were not consistent concerning age and gender. Contrary to Narkwa et al. in Ghana, Vairo et al. described an association between age and DENV infection in blood donors in Zanzibar: they reported an odds ratio of 1.42 for every increase in donor age of 5 years. However, an association between the male gender and DENV infection has been described by the Ghanaian authors. These contradictory findings are also described in non-blood donors.[8,13,32,34]

In Burkina Faso, very few studies on DENV in blood donors has been conducted in 2003.[35] This study reported a higher prevalence of DENV infection among blood donors in rural areas than in urban areas (34.8% vs 30.4%). In pregnant women included in the same study, the prevalence of DENV infection was two times higher in urban areas compared to the prevalence in rural areas (39% vs 22.5%).

Although the WHO recommends blood services to define, with regard to their epidemiological context, relevant measures to exclude risky donors from blood donation, the fact is that our knowledge is old and not very up to date. Despite Burkina Faso experiencing repeated dengue fever outbreaks (2013, 2015 and 2016) with an increased number of cases each time, the establishment of a routine surveillance system occurred only at the end of the last quarter of 2016. As a result, there were no reliable data on DENV to enable the National blood transfusion centre (CNTS) to take appropriate measures. Therefore, it seems necessary to update the seroprevalence and factors associated with anti-DENV antibody positivity among blood donors and to discuss their implications for blood supply.

1 | MATERIAL AND METHODS

1.1 | Study design and setting

1.1.1 | Study area

Burkina Faso, located in West Africa, is part of the Soudano-Sahelian area, with a rainy season from May to October (with a mean temperature of 28°C or 82 °F) and a dry season comprised of a cold period from December to February (minimum average temperature of 16°C or 61 °F) and a hot one, which runs from March to May, when the temperature can reach as high as 43°C or 109 °F.[36]

With an estimated population of 19 034 397 in 2016,[37] the country is mainly rural; only about 29% of the population lived in urban areas in 2014. However, Burkina Faso is urbanising rapidly and is the fourth country with the fastest urbanisation in the last quarter of a century.[38] Ouagadougou, the country and central region's capital city, with around 2.8 million inhabitants is the largest city of the country. Its population increased from 282 000 inhabitants in 1985 to 709 000 inhabitants in 1996 and to 2 637 303 inhabitants in 2016, concomitant with spectacular spatial growth.[33,37] The major part of this spatial expansion can be described in terms of "peripheral urbanisation". Indeed, next to the planned urbanisation with the parcelled neighbourhoods, there are non-parcelled neighbourhoods ("*non-lotis*") that lack basic supply infrastructures (water supply, sanitation, *etc*.). The city is divided into 12 districts and 52 sectors. Except Bobo-Dioulasso (nearly a million inhabitants) and Ouagadougou, the other parts of the country are essentially semi-urban to rural. Living conditions are characterised by precarious housing, with 72% of households living in "*non-lotis*" areas and only 8% having access to adequate sanitation.[39]

Burkina Faso has put in place a centralised blood transfusion system, with the CNTS, the unique operator, which collects and distributes blood in the country through a network of four regional blood transfusion centres (CRTS) located in Ouagadougou, Bobo-Dioulasso, Koudougou and Fada N'Gourma. The CRTS of Ouagadougou (CRTS-O) is the biggest one and covers six administrative regions (Figure 1) that account for around 8.8 million inhabitants (46.2% of the total population). It collects around 40 000 blood units per year from voluntary unpaid blood donors at one fixed site (in Ouagadougou) and multiple mobile sites, mainly in Ouagadougou and some other localities of the catchment area. About 75% of blood units come from mobile collections. During the rainy season, due to the recrudescence of malaria cases (the

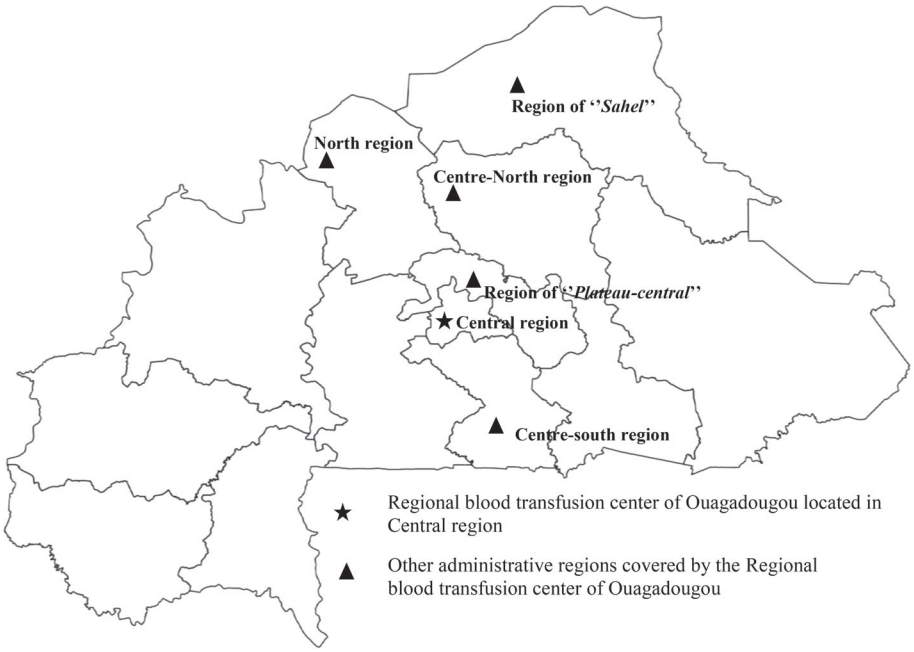

FIGURE 1 Regional blood transfusion centre of Ouagadougou and its coverage areas

main indication of blood transfusion in children and pregnant women), the CRTS-O organises many mobile blood collections throughout its catchment area. From November, mobile collections are more focused on Ouagadougou and its immediate surroundings because of the decrease in blood demand and the scarcity of financial resources by the year end to support outings in remote areas.

Red cell concentrate (RCC), platelet concentrate (PC) and frozen fresh plasma (FFP) are processed from whole blood collected from and delivered to five teaching hospitals (four in Ouagadougou and one in Ouahigouya), two regional hospitals (Kaya and Dori) and several district hospitals and private medical facilities in the six administrative regions.

1.1.2 | Study design

We conducted a 4-week cross-sectional study at the end of the 2016 dengue fever outbreak in Burkina Faso, from December 4 to 30, 2016.

1.2 | Study population and sampling

1.2.1 | Inclusion criteria

Blood donors of both genders, aged 18-60 years, accepted for blood donation after medical selection were consecutively enrolled, irrespective of collection site (fixed or mobile) and living area (urban or rural). Blood collections were scheduled 1 or 2 months in advance in Ouagadougou (Central region) and the five other administrative regions, i.e. "*Plateau central*", North Central, South Central, North and "*Sahel*" (Figure 1).

The medical selection was performed by trained staff using a pre-donation questionnaire focused on risk behaviours for HIV and hepatitis B and C viruses, as well as signs and situations suggestive of infectious or non-infectious diseases. Thus, histories of fever and treatments with antibiotics or anti-malarial drugs were checked during the pre-donation interview. Donors with a positive questionnaire were excluded from blood donation.

In addition to the blood units collected, a venous blood sample was drawn from each volunteer donor for serological screening. The samples were sent to the laboratory of CRTS-O for routine screening tests (HIV, HBV, HCV and syphilis). A serum of each sample was aliquoted within 12 hours after phlebotomy, frozen at − 80°C for later screening for IgG anti-DENV.

Any blood unit that tested positive for HIV, hepatitis B or C virus or syphilis was discarded. Only non-infected processed blood components (RCC, PC and FFP) were considered for appreciation of the implications of DENV on blood supply.

1.2.2 | Sample size calculation

Assuming that the prevalence of DENV antibodies in Burkina Faso, irrespective of areas, was 50%, we estimated the required sample size with $\alpha = 5\%$ and absolute precision of 0.03 to be 1067. The formula for the calculation of the sample size was applied as previously described.[40]

1.3 | Study variables

The dependent variable in this study was the result (positive or negative) of the DENV IgG antibody test.

The independent variables were age group (under 20, 20-29, 30-39, 40-49 and over 50 years), gender (male or female), living area

(urban or rural), donor status (first-time or repeated blood donor) and collection site (fixed or mobile).

1.4 | Serological tests

The serum sample obtained from each donor was analysed by serological tests. We used ARCHITECT HIV Ag/Ab Combo kits (ABBOTT, Wiesbaden Germany), ARCHITECT HBsAg Qualitative II (ABBOTT Ireland, Sligo Ireland) and ARCHITECT Anti-HCV (ABBOTT GmbH & Co.KG, Wiesbaden Germany) to detect, respectively, surface antigen of HBV, antibodies anti-HIV 1 and 2 and P24 antigen and antibodies for anti-HCV. For syphilis, Rapid Plasma Reagin, -RPR-Carbon- (Spinreact, Ctra.Santa Coloma, Spain) was used.

In addition, serum samples of the included individuals were first tested in singlicate for dengue IgG antibodies using an IgG indirect ELISA, PanBio Dengue IgG Indirect ELISA (Brisbane, Australia). Initial reactive or equivocal samples were retested in duplicate. The results were interpreted using a spreadsheet provided by the manufacturer and expressed in "PanBio units". The test was negative for a result <9, equivocal if 9-11 and positive if ≥11. The sample was considered positive for IgG anti-DENV if it was reactive at least twice, i.e. initial reactivity and at least one reactivity in duplicate retest or equivocal at initial test and reactive at both duplicate retests. The other situations were discordant tests, and samples were considered negative.

All these tests (routine tests and IgG anti-DENV ELISA test) have been used according to the manufacturer's instructions.

1.5 | Study definitions

The city of Ouagadougou (the central region) was considered an urban area, and the other administrative regions (i.e. "*Plateau central*", North Central, South Central, North and "*Sahel*") were considered rural areas (Figure 1).

Repeated donor was defined as a donor who already donated blood at least once prior to the start of the study.

Positivity to IgG anti-DENV indicated that the subject has been in contact with the DENV. IgG anti-DENV alone does not discriminate recent infection from an old one.

1.6 | Statistical analysis

Data were entered in Microsoft Excel 2000 and exported to STATA 13 for analyses.

First, we used proportions and mean ± 2 standard deviation (SD) to describe our study population. Associations between IgG anti-DENV positivity and dependent factors were tested using odds ratios (OR) and χ^2 test. We performed a multivariate logistic regression. All variables with a *P*-value < .20 at univariate analysis were included in the model. All differences were considered significant at *P*-values <.05.

1.7 | Ethical considerations

The study was authorised by the Internal Scientific Review Committee of the CNTS. Blood donors gave informed consent for serological

TABLE 1 Baseline characteristics of blood donors recruited from urban and rural areas in 2016 in Burkina Faso

Variable	Overall n (%)	Urban area n (%)	Rural area n (%)	*P*-value
Total included	1007 (100)	787 (78.2)	220 (21.8)	—
Age (Mean ± sd)	26.1 ± 8.1	27.1 ± 8.7	22.6 ± 4.4	.000
Age group (years)				.000
<20	115 (11.4)	81 (10.3)	34 (15.4)	
20-29	649 (64.4)	476 (60.5)	173 (78.6)	
30-39	153 (15.2)	144 (18.3)	9 (4.1)	
40-49	68 (6.7)	64 (8.1)	4 (1.8)	
>50	22 (2.2)	22 (2.8)	0 (0)	
Gender				.295
Male	638 (63.4)	492 (62.5)	146 (66.4)	
Female	369 (36.4)	295 (37.5)	74 (33.6)	
Donor status				.000
First-time donor	599 (59.5)	409 (52.0)	190(86.4)	
Repeated donor	408 (40.5)	378 (48.0)	30 (13.6)	
Collection site				.000
Fixed	153 (15.2)	150 (19.1)	3 (1.4)	
Mobile	854 (84.8)	637 (80.9)	217 (98.6)	
IgG anti-DENV				.000
Positive	721 (71.6)	600 (76.2)	121 (55.0)	
Negative	286 (28.4)	187 (23.8)	99 (45)	

TABLE 2 Univariate analysis of factors associated with IgG anti-DENV antibody positivity among 1007 blood donors in Burkina Faso in 2016

Variable	Positive n (%)	OR	IC 95%	*P*-value
Age group				
<20	70 (60.9)	1	—	—
20-29	453 (69.8)	1.48	0.98-2.24	.06
30-39	122 (79.7)	2.53	1.47-4.36	.001
40-49	57 (83.8)	3.33	1.58-7.02	.002
>50	19 (86.4)	4.07	1.14-14.55	.03
Female gender	270 (73.2)	1.13	0.85-1.51	.4
Residence in rural area	121 (55.0)	0.38	0.28-0.52	.000
First-time donor	314 (77.0)	0.63	0.48-0.84	.002
Mobile collection	591 (69.2)	0.40	0.25-0.63	.000

TABLE 3 Multivariate logistic regression of independent predictors for IgG anti-DENV antibody positivity among 1007 blood donors in Burkina Faso in 2016

Predictors	OR	IC 95%	*P*-value
Residence in rural area	0.47	0.33-0.65	.000
Age group			
<20	1	—	—
20-29	1.38	0.91-2.10	.13
30-39	1.86	1.06-2.55	.03
40-49	2.35	1.10-5.05	.03
>50	2.70	0.74-9.81	.13
Mobile blood collection	0.58	0.35-0.94	.03
First-time donor	0.93	0.68-1.29	.69

testing. Data have been collected anonymously. Confidentiality and dignity of the included subjects have been preserved.

2 | RESULTS

Our study included a total of 1007 blood donors. Donors from urban areas represented 78.2%. The mean age was 26.1 ± 8.1 years. Blood donors from rural areas were younger than those from urban areas (Table 1). Antibodies for anti-DENV IgG were found in 71.6% (n = 721) of donors. The prevalence of IgG anti-DENV was significantly higher ($P < .001$) in urban areas (76.2%) compared to rural settings (55.0%) as shown in Table 1.

A total of 1007 blood units were collected from the study population (each donor donating one unit). Due to positive results for HIV, HBV, HCV or syphilis, 137 (13.6%) blood units were discarded. The remaining 870 units have been processed into 1056 blood components (RCC, PC and FFP), which have been delivered to patients. Of these 1056 blood components, 801 units (75.8%) were positive for IgG anti-DENV.

In univariate analysis (Table 2), donors aged 30-39 years (OR = 2.53; $P = .001$), 40-49 years (OR = 3.33; $P = .002$) and above 50 years (OR = 4.07; $P = .03$); living in rural areas (OR = 0.38; $P = 0.000$); being first-time donor (OR = 0.63; $P = .002$); and attending a mobile collection site (OR = 0.4; $P = .000$) were associated with the positivity to IgG anti-DENV.

After adjustment in a multiple regression logistic model, age, living area and collection sites were found to be independent predictors of IgG anti-DENV in blood donors as shown in Table 3. Compared to those younger than 20 years, donors aged 30-39 and 40-49 years had 1.8 (OR = 1.86; $P = .03$) and 2.3 (OR = 2.35; $P = .03$) times higher odds of having a positive IgG anti-DENV test, respectively.

The odds of DENV (Table 3) was 53% lower in rural areas compared to urban settings (OR = 0.47, CI = 0.33-0.65, $P = .000$) and 42% lower in mobile sites compared to fixed ones (OR = 0.58, CI = 0.35-0.94, $P = .03$).

3 | DISCUSSION

3.1 | Limitations

Our study is the second known of its kind that was carried out in Burkina Faso. Conducted some 15 years after the first one, it allows an update of data on DENV in blood donors. However, it has some limitations. First, our sample included a high proportion of donors from urban areas and from mobile collection sites; this is related to the period of our study (more frequent organisation of mobile blood collections inside Ouagadougou). Thus, it was less representative of the donor population in Burkina Faso. Therefore, this prevalence cannot be generalised to all donors. Second, we did not perform an antibody neutralising assay to rule out cross-reactions with other circulating flaviviruses. Indeed, as previous studies indicate regarding the circulation of other flaviviruses,[33] the plaque reduction neutralisation test (PRNT) could have allowed us to determine antibody and serotype specificity. Moreover, it would have been necessary to perform a nucleic acid test (NAT) or at least serological tests for NS1Ag and IgM anti-DENV to attempt to identify recent (primary or secondary) infections that are the most important concern for blood safety. At the time of the study, the plaque reduction neutralisation test and NAT were not available in Burkina Faso.

3.2 | Seroprevalence of IgG anti-DENV

We found a 2.2-times increase in the prevalence of IgG anti-DENV, from 32.5% (in 2003) to 71.6% (current study). Compared to the previous study,[35] which reported a prevalence of IgG anti-DENV of 30.4% in Ouagadougou versus 34.8% in a rural area (Nouna), we found a higher seroprevalence ($P < .001$) in urban areas (76.2%) than in rural areas (55.0%). The prevalence in Ouagadougou increased by 150%. These findings were expected and reflect the cumulative results of the different epidemics that occurred since 2003. Dengue fever outbreaks were declared in Burkina Faso in 2013, 2015[7,8,13] and 2016.[14,36] Therefore, as only IgG antibodies were screened, our study detected all donors who have ever been in contact with DENVs, either before or during the 2016 outbreak, and who still have a detectable title of circulating IgG anti-DENVs.

We found higher prevalence compared to some other African countries that are not reported to have experienced recent outbreaks (50.6% in Tanzania and 43.6% in Ghana).[30,31]

3.3 | Factors associated with IgG anti-DENV positivity in blood donors

In univariate and multivariate analyses, residence in rural area was negatively associated with dengue infection. Donors living in rural areas were 50% less likely to have a positive IgG anti-DENV test than those living in Ouagadougou (OR = 0.47; IC = 0.33–0.65, $P = 0.000$). Vairo et al.[33] in Zanzibar, reported that donors living in urban areas were three time more likely to be infected. These findings show the role of geographical factors in the susceptibility of different mosquito species to DENV. This susceptibility varies geographically as shown by Armstrong & Rico-Hesse.[41] The profile observed in our study is consistent with the geographical context in our country. It is well established that rapid and unplanned demographic and societal changes, such as population growth, urbanisation and modern transportation, could lead to an increased transmission of DENV by increasing the vector population and changing the ecological balance of different species.[42] Ouagadougou, similar to other African cities, has experienced an exponential urbanisation these last 20 years. The population grew annually by 7.6% in Ouagadougou versus 3.1% in the rest of the country.[43] This rapid urbanisation increases the population density and the risk of having informal settlements that can be associated with increased risk of dengue infection as stagnant waters inside and out of the concessions and poor sanitation provide an environment for *Aedes aegypti* proliferation in close proximity to human hosts. Previous studies showed that the presence of waste in the environment is a significant risk factor for flavivirus infections because empty plastic containers constitute peri-domestic breeding sites for *Aedes aegypti* during the rainy season. In addition, dumpsters, where they exist, are not regularly emptied, providing breeding sites for vectors.[33]

Donors aged 30-39 years (OR = 1.86; IC = 1.06-2.55, $P = .03$) and 40-49 years old (OR = 2.35; IC = 1.10-5.05, $P = .03$) were more likely to be infected compared to younger donors. These findings are consistent with the reports in literature.[30] They could be explained by repeated exposures over the time, to the risk of infection, for older donors. The recent campaigns for malaria control (free distribution of long-lasting insecticide-treated mosquito nets) could have been more beneficial to the younger population and protected them against *Aedes aegypti* bites compared to older ones, which were already exposed before.

3.4 | Implications and recommendations for safe blood supply

Around two thirds of the world are now endemic for dengue, with an increasing likelihood that blood donors in those countries are infected. This could impact blood supply in two ways.

First, dengue mainly affects the youth and young adults, the segment of population that donates blood. So, this will result in a significant reduction in the donor population as the infected subjects could present clinical symptoms (hyperthermia, headache, *etc*.) that exclude them from donation. These symptomatic forms sometimes reach 50%.[16] Because DENV outbreaks are increasing in magnitude and frequency over time, their effect on donors' attendance may be enough to negatively impact blood supply. For example, in Singapore, the 2007 dengue outbreak resulted in a decrease of the blood donor pool by 0.2-1.1%.[44]

Second, as DENV is transmitted via arthropod bite, it remains present in the bloodstream for a few days; this implies at least a theoretical risk of transmission via blood products.[3] DENV is a part of the emerging risks of transfusion-transmitted infections with the WNV and the Chikungunya virus (CHIKV) among others.[3,45] Transmission of DENV through viraemic blood products is currently well documented.[21,27-29] This risk is related to asymptomatic or subclinical cases.

In our study, 801 (75.8%) of the 1056 blood components processed were positive for IgG anti-DENV. The serological tests used did not allow us to discriminate between a recent infection and an old one: we cannot objectively appreciate the risk to recipients of blood products. However, studies using NAT tests in dengue-endemic areas estimated a transmission rate of up to 37% in recipients who received viraemic blood products.[21,25]

To mitigate the risk of transmission of DENV through blood components, many strategies could be implemented according to whether the country is endemic or not for DENV as shown in Table 4. Some non-endemic countries such as Australia, France and the United States restrict donations from “at-risk” donors (blood donors returned from dengue-endemic areas) if RCC, PC or therapeutic FFP are expected to be processed. Similar measures taken to mitigate CHIKV in Singapore resulted in the exclusion of almost 3-4% of donors, in addition to those who are self-excluded because they have symptoms and those who are excluded for other reasons.[44] This strategy of restricting fresh component collection from “at-risk” donors appears to be an effective method for reducing the risk of TT-DENV in Australia,[45] but it will be useless in endemic areas where many studies demonstrated that it was not effective.[44]

TABLE 4 Possible strategies to mitigate transfusion-transmitted risk of dengue virus in endemic and non-endemic areas[6,44,45]

Strategy	Endemic area	Non-endemic area	Comments/suggestions
Exclusion of symptomatic blood donors	Indicated	Indicated	Possibly ineffective due to high proportion of asymptomatic cases
Temporarily exclusion of at-risk donors	Donors from parts of country with high cases during outbreak	Exclusion for at least 4 weeks of donors returning from endemic area	Could be effective but with high negative impact on blood supply. Blood services must develop new strategies to recruit enough not at-risk donors
Active tracking of post-donation information about suggestive signs	Indicated	Indicated	Possibly ineffective due to high proportion of asymptomatic cases
NAT DENV test	Indicated	Non-indicated	Identification of viraemic blood donors. Costly strategy for resource-limited endemic countries
screening for AgNS1 or IgM	Indicated	Non-indicated	Detection of recent infections. Reagent kit with good sensibility and specificity must be selected
Pathogen reduction techniques	Indicated	Indicated	Inactivation or reduction of a wide range of pathogens, including those that are still unidentified. This strategy could be the way forward to reduce cost by allowing the lightening/removing of certain biological tests and process of securing blood. But for the moment, it is a costly strategy for resource-limited endemic countries.

Other measures used in developed countries to mitigate the risk of TT-DENV are pathogen reduction technologies (PRTs) and NAT.[3,44-46] However, these measures are currently out of reach for developing countries. However, for these countries that are known to be multi-endemic to many pathogens, PRTs represent the best way forward, both to improve the safety of blood products and to reduce their production costs. These technologies are not the panacea for now (cumbersome process, potential inefficiency on some pathogens such as parvoviruses and prions); however, they address around 95% of existing and emerging pathogens, providing interesting prospects for lightening or removing of certain donor selection criteria and even some biological screening tests and blood products' irradiation.[47]

Waiting for this "technological revolution", an alternative approach of mitigating DENV in our context may be to screen all donors for recent infections. A study conducted in Australia showed that the detection of the DENV NS1 antigen could be suitable for detecting asymptomatic and recent infections in blood donors.[45] However, implementing this strategy in developing countries could impact the sustainability of blood service and may not be cost-effective.

In the specific case of Burkina Faso, given that DENV is still mainly limited to urban areas, blood services could temporarily exclude these areas for blood collection. In return, they must increase the number of blood collections in rural areas in order to maintain the level of blood supply.

4 | CONCLUSION

Until the 2016 outbreak, dengue was a neglected disease in Burkina Faso. No particular measure, even the measurement of body temperature in blood donors, was implemented to reduce the risk of TT-DENV. Due to the recurrence of outbreaks, there is a need for evidence to guide action and control the situation. Our study provides new and useful information about DENV in blood donors. It provides insights for future research on the risk of TT-DENV. In particular, these findings call for a better definition of the seroprevalence of DENV in blood donors and a response plan to mitigate TT-DENV risk and secure blood supply. These actions must take into consideration the proportion of viraemic asymptomatic blood donors and the cost-effectiveness of NS1Ag and IgM screening during outbreaks.

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CONFLICT OF INTEREST

The authors have no competing interests.

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REFERENCES

1. Jahan NK, Ahmad MP, Dhanoa A, et al. A community-based prospective cohort study of dengue viral infection in Malaysia: the study protocol. *Infect Dis Poverty*. 2016;5:1-9. https://doi.org/10.1186/s40249-016-0172-3.

2. Messina JP, Brady OJ, Scott TW, et al. Global spread of dengue virus types: mapping the 70 year history. *Trends Microbiol*. 2014;22(3):138-146.
3. Pozzetto B, Memmi M, Garraud O. Is transfusion-transmitted dengue fever a potential public health threat? *World J Virol*. 2015;4(2):113-123.
4. Amarasinghe A, Kuritsky JN, Letson W, Margolis HS. Dengue virus infection in Africa. *Emerg Infect Dis*. 2011;17(8):1349-1354.
5. Were F. The dengue situation in Africa. *Paediatr Int Child Health*. 2012;32(suppl 1):18-21.
6. Wilder-Smith A, Chen LH, Massad E, Wilson ME. Threat of dengue to blood safety in dengue-endemic countries. *Emerg Infect Dis*. 2009;15(1):8-11.
7. Ridde V, Agier I, Bonnet E, et al. Presence of three dengue serotypes in Ouagadougou (Burkina Faso): research and public health implications. *Infect Dis Poverty*. 2016;5(23):1-13. https://doi.org/10.1186/s40249-016-0120-2.
8. Ridde V, Carabali M, Ly A, et al. The need for more research and public health interventions on dengue fever in Burkina Faso. *PLoS Negl Trop Dis*. 2014;8(6):e2859. https://doi.org/10.1371/journal.pntd.0002859.
9. Murray NE, Quam MB, Wilder-Smith A. Epidemiology of dengue: past, present and future prospects. *Clin Epidemiol*. 2013;5:299-309.
10. Gonzales J-P, Du Saussay C, Gautun J-C, McCormick J, Mouchet J. La dengue au Burkina Faso (ex-Haute-Volta): épidémies saisonnières en milieu urbain à Ouagadougou. *Bull Soc Pathol Exotique*. 1985;78(1):7-14.
11. Franco L, Di Caro A, Carletti F, et al. Recent expansion of dengue virus serotype 3 in West Africa. *Euro Surveill*. 2010;15(7):1-4. https://doi.org/pii=19490.
12. Eldin C, Gautret P, Nougairede A, et al. Identification of dengue type 2 virus in febrile travellers returning from Burkina Faso to France, related to an ongoing outbreak, October to November 2016. *Eur Secur*. 2016;21(50):1-3. https://doi.org/10.2807/1560-7917.ES.2016.21.50.30425.
13. Tarnagda Z, Congo M, Sagna T, et al. Outbreak of dengue fever in Ouagadougou, Burkina Faso, 2013. *Int J Microbiol Immunol Res*. 2014;2(7):101-108.
14. Tarnagda Z, Cissé A, Bicaba BW, et al. Dengue fever in Burkina Faso, 2016. *Emerg Infect Dis*. 2018;24(1):170-172.
15. Tsai J-J, Lin P-C, Tsai C-Y, Wang Y-H, Liu L-T. Low frequency of asymptomatic dengue virus-infected donors in blood donor centers during the largest dengue outbreak in Taiwan. *PLoS One*. 2018;13(10):e0205248. https://doi.org/10.1371/journal.pone.0205248.
16. Linnen JM, Vinelli E, Sabino EC, et al. Dengue viremia in blood donors from Honduras, Brazil, and Australia. *Transfusion*. 2008;48(7):1355-1362.
17. Petersen LR, Tomashek KM, Biggerstaff BJ. Estimated prevalence of dengue viremia in Puerto Rican blood donations, 1995 through 2010: prevalence of dengue viremic donations. *Transfusion*. 2012;52(8):1647-1651.
18. Stramer SL, Linnen JM, Carrick JM, et al. Dengue viremia in blood donors identified by RNA and detection of dengue transfusion transmission during the 2007 dengue outbreak in Puerto Rico: dengue transfusion transmission. *Transfusion*. 2012;52(8):1657-1666.
19. Ashshi AM. Serodetection of dengue virus and its antibodies among blood donors in the western region of Saudi Arabia: a preliminary study. *Blood Transfus*. 2015;13:135-138.
20. Ashshi AM. The prevalence of dengue virus serotypes in asymptomatic blood donors reveals the emergence of serotype 4 in Saudi Arabia. *Virol J*. 2017;14(107):1-8. https://doi.org/10.1186/s12985-017-0768-7.
21. Sabino EC, Loureiro P, Lopes ME, et al. Transfusion-transmitted dengue and associated clinical symptoms during the 2012 epidemic in Brazil. *J Infect Dis*. 2016;213(5):694-702.
22. Ribas-Silva RC, Eid AA. Dengue antibodies in blood donors. *Rev Bras Hematol Hemoter*. 2012;34(3):193-195.
23. Biggerstaff BJ, Petersen LR. Estimated risk of West Nile virus transmission through blood transfusion during an epidemic in Queens, New York City. *Transfusion*. 2002;42(8):1019-1026.
24. Biggerstaff BJ, Petersen LR. Estimated risk of transmission of the West Nile virus through blood transfusion in the US, 2002: transfusion risk of West Nile virus, 2002. *Transfusion*. 2003;43(8):1007-1017.
25. Seed CR, Kiely P, Hyland CA, Keller AJ. The risk of dengue transmission by blood during a 2004 outbreak in Cairns, Australia. *Transfusion*. 2009;49(7):1482-1487.
26. Chuang VW, Wong T, Leung Y, et al. Review of dengue fever cases in Hong Kong during 1998 to 2005. *Hong Kong Med J*. 2008;14(3):170-177.
27. Tambyah PA, Koay ESC, Poon MLM, Lin RVTP, Ong BKC. Dengue hemorrhagic fever transmitted by blood transfusion. *N Engl J Med*. 2008;359(14):1526-1527.
28. Levi JE, Nishiya A, Félix AC, et al. Real-time symptomatic case of transfusion-transmitted dengue: dengue transmission by transfusion. *Transfusion*. 2015;55:961-964.
29. Oh HB, Muthu V, Daruwalla ZJ, Lee SY, Koay ES, Tambyah PA. Bitten by a bug or a bag? Transfusion-transmitted dengue: a rare complication in the bleeding surgical patient: dengue transmission from a blood transfusion. *Transfusion*. 2015;55(7):1655-1661.
30. Vairo F, Nicastri E, Yussuf SM, et al. IgG against dengue virus in healthy blood donors, Zanzibar, Tanzania. *Emerg Infect Dis*. 2014;20:465-468.
31. Narkwa PW, Mutocheluh M, Kwofie TB, et al. Dengue virus exposure among blood donors in Ghana. *J Med Biomed Sci*. 2016;5(2):30-35.
32. Eldigail MH, Adam GK, Babiker RA, et al. Prevalence of dengue fever virus antibodies and associated risk factors among residents of El-Gadarif state, Sudan. *BMC Public Health*. 2018;18(1):921. https://doi.org/10.1186/s12889-018-5853-3.
33. Fournet F, Rican S, Vaillant Z, et al. The influence of urbanization modes on the spatial circulation of Flaviviruses within Ouagadougou (Burkina Faso). *Int J Environ Res Public Health*. 2016;13(1226):1-14. https://doi.org/10.3390/ijerph13121226.
34. Rafique I, Saqib MAN, Munir MA, et al. Asymptomatic dengue infection in adults of major cities of Pakistan. *Asian Pac J Trop Med*. 2017;10(10):1002-1006.
35. Collenberg E, Ouedraogo T, Ganamé J, et al. Seroprevalence of six different viruses among pregnant women and blood donors in rural and urban Burkina Faso: a comparative analysis. *J Med Virol*. 2006;78(5):683-692.
36. Lim JK, Carabali M, Lee J-S, et al. Evaluating dengue burden in Africa in passive fever surveillance and seroprevalence studies: protocol of field studies of the dengue vaccine initiative. *BMJ Open*. 2018;8:1-14. https://doi.org/doi:10.1136/bmjopen-2017-017673.
37. INSD, Institut National de la Statistique et de la Démographie. Projections démographiques de 2007-2020. Ministère de l'Economie et des Finances; 2009. www.insd.bf/n/...?/Projections_demographiques_sous_nationales_2007-2020.pdf
38. United Nations. Department of Economic and Social Affairs, population. World urbanization prospects, the 2014 revision (ST/ESA/SER.A/366); 2015. https://esa.un.org/unpd/wup/publications/files/wup2014-report.pdf
39. INSD, Institut National de la Statistique et de la Démographie. *Enquête multisectorielle continue (EMC) 2014: Habitat, assainissement et accès à l'eau potable* (p. 49). Ministère de l'Economie et des Finances; 2015. http://www.insd.bf/n/contenu/enquetes_recensements/Enq_EMC/Habitat_Assainissement_et_Acces_a_eau.pdf
40. Brown WS, Newman TB, Hulley SB, eds. Estimating sample size and power: applications and examples. *Designing Clinical Research*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007.

41. Armstrong PM, Rico-Hesse R. Efficiency of dengue serotype 2 virus strains to infect and disseminate in *Aedes aegypti*. *Am J Trop Med Hygiene*. 2003;68(5):539-544.
42. Gubler DJ. Epidemic dengue/dengue hemorrhagic fever as a public health, social and economic problem in the 21st century. *Trends Microbiol*. 2002;10(2):100-103.
43. Dupuis B, Leu P, Söderström O, Biehler A. La mondialisation des formes urbaines à Ouagadougou, troisième partie; 2010. https://www.unine.ch/...?ouaga/3_La_mondialisation_des_formes_urbaines_a_Ouagadougou_troisieme_partie.pdf
44. Teo D, Ng LC, Lam S. Is dengue a threat to the blood supply? *Transfus Med*. 2009;19(2):66-77.
45. Rooks K, Seed CR, Fryk JJ, et al. Mitigating the risk of transfusion-transmitted dengue in Australia. *J Blood Transfus*. 2016;2016:1-6. https://doi.org/10.1155/2016/3059848.
46. Faddy HM, Seed CR, Fryk JJ, et al. Implications of dengue outbreaks for blood supply, Australia. *Emerg Infect Dis*. 2013;19(5):787-789.
47. FDA, Food and Drug Administration. FDA addresses efforts to promote blood product pathogen-reduction technologies; 2019. https://www.infectioncontroltoday.com/fda/fda-addresses-efforts-promote-blood-product-pathogen-reduction-technologies

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